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Pathology

EXPERIMENTAL PATHOLOGY

1177. **The Development of Histiocytes and Macrophages from Lymphocytes**

H. DOWNEY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 499–507, April, 1955. 38 refs.

At the Medical School of the University of Minnesota the author has studied the different stages in the development of histiocytes from lymphocytes in the omentum, lymph nodes, and spleen of rats and rabbits after the animals had been given intravenous and intraperitoneal injections of different irritant substances. Smears of human peritoneal exudate were also examined.

This study has enabled the author to verify the conclusions drawn from the classic experiments in this field. He found that the extent of the emigration of lymphocytes and their development into histiocytes depended on the severity of the inflammatory reaction and the ability of the tissues involved to supply lymphocytes with histiocytic potential from their own cells. In acute conditions few lymphocytes from lymphoid organs were transformed into histiocytes, probably because of the presence of active reticulum, though when a severe inflammatory reaction persisted there might be extensive involvement of lymphocytes. *J. B. Wilson*

1178. **Experimental Approach to the Pathogenesis of Retrolental Fibroplasia. II. The Influence of the Developmental Maturity on Oxygen-induced Changes in the Mouse Eye**

L. J. GYLLENSTEN and B. E. HELLSTRÖM. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **39**, 475–488, April, 1955. 20 figs., 28 refs.

Since it is a well-established fact that immaturity of the organism is a predisposing factor in determining the onset of retrolental fibroplasia, the authors have attempted, in experiments on mice at the Karolinska Institute, Stockholm, to assess the influence of age at the time of exposure to oxygen upon the pathological changes which ensue on transfer to air.

Newborn, 5-day-old, and 10-day-old mice were exposed to 98–100% oxygen continuously for 5 days, then rapidly transferred to air and batches killed after intervals of 1, 2, 5, and 10 days, when the eyes were examined histologically. Ocular haemorrhages, retinal vasoproliferation, and irregularities of the retinal layers were found in all groups of mice, but haemorrhages and retinal vasoproliferation were more marked in the younger animals than in the older ones. On the other hand the older animals showed a higher incidence of retinal irregularities and an increasing frequency of a characteristic retinal atrophy of the ganglion-cell layer, the inner nuclear layer, and the outer plexiform layer. In newborn mice the retinal changes were largely confined to the optic disk, whereas in the older animals they reached more anteriorly.

The similarity of these findings to those in retrolental fibroplasia is pointed out; however, the important differences are also stressed, and a warning is given of the dangers of drawing too close an analogy between the mechanisms involved in these animal experiments and in the genesis of the human disease. *Norman Ashton*

1179. **Experimental Oesophagitis in Rats**

K. V. LODGE. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **36**, 155–161, April, 1955. 6 figs., 5 refs.

In a recent post-mortem study of non-specific oesophagitis (*Thorax*, 1955, **10**, 56; *Abstracts of World Medicine*, 1955, **18**, 288) the author found that the lesion occurred much more frequently than has been generally recognized. It appeared that conditions favouring excessive contact between the gastric contents and the oesophageal epithelium predisposed to the development of oesophagitis. A number of previous workers on gastric ulcer have noted that ulcers developed in the proventriculus of starved rats and have suggested that a deficiency of some factor in the diet, such as protein, was responsible for the ulceration. But what these workers have failed to appreciate is that the proventriculus is lined with squamous epithelium and acts as a food reservoir, being essentially a dilated portion of the oesophagus.

In the studies now described the author maintained rats in good condition for up to 3 weeks on a diet of glucose and sodium chloride solution without solid food. On this partial starvation diet, which was totally deficient in protein, ulceration occurred in the oesophagus and the proventriculus of the rats, but death from starvation did not occur, and it was thus possible to kill them in batches at predetermined intervals so that stages in the development of the lesion could be studied. The findings suggested that the inflammatory oesophageal lesion which occurred in these rats was due to the reduction in *p*H of the gastric juice. This was confirmed by the absence of ulceration when this fall in gastric *p*H was prevented by the addition of sodium

bicarbonate to the diet, and indeed this addition produced healing of ulcers already established.

In further experiments the performance of vagotomy and muscle resection designed to cause reflux of gastric contents from the proventriculus into the oesophagus provided additional proof of the importance of gastric acid in the production of oesophagitis, for the vagotomy, despite continuation of the diet of glucose and salt solution only, reduced the amount of acid secreted and no inflammation or ulceration occurred. However, on the addition of dilute hydrochloric acid and pepsin to the diet ulceration again developed.

In the author's previous study of human subjects it appeared that oesophagitis occurred when there had been incompetence of the cardio-oesophageal junction due to such local causes as prolonged gastric intubation or to general causes such as loss of muscle tone and decubitus, or a history of persistent vomiting, conditions which exposed the squamous epithelium of the oesophagus to excessive contact with the gastric juice. The author now claims that the experimental evidence presented here supports this theory of the pathogenesis of non-specific oseophagitis in man and suggests that hyperchlorhydria may be an additional causative factor.

[See also Abstract 1203.] *E. Forrai*

1180. **Experimental Induction of Gastric Ulcer by Irritation in the Region of the Duodenum.** (Механизм образования экспериментальных язв желудка, вызванных нанесением чрезмерного раздражения на область двенадцатиперстной кишки)

I. S. Zavodskaya. *Фармакология и Токсикология* [*Farmakol. i Toksikol.*] **18**, 37–41, March–April, 1955. 2 figs., 2 refs.

In the study here described irritation of the duodenum of guinea-pigs was achieved either mechanically or chemically during laparotomy under light ether anaesthesia, the mechanical irritation being produced by means of a haemostatic clamp applied to the duodenum for 10 minutes and chemical irritation by the injection of 0·2 ml. of alcohol or turpentine into the muscle layer of the duodenal wall. The laparotomy incision was then closed and the animals killed at various intervals from one to 24 hours thereafter.

Post-mortem examination revealed the presence of oedema, haemorrhages, leucocytic infiltration, mucosal necrosis, erosions, even ulceration of the stomach wall, these changes being observable as early as 3 to 6 hours after the operation. Ulceration was most marked in areas distant from the site of irritation, that is, in the fundus and prepyloric region. Since great care was taken not to damage directly the vessels of the pyloro-duodenal region, the author considers it highly improbable that the lesions could have been due to direct trauma of the gastric vessels.

Subsequent experiments on rabbits and rats showed that preliminary sub-diaphragmatic section of both vagus nerves prevented almost completely this post-traumatic gastric ulceration. The author also succeeded in reproducing the process on a dog with a Pavlov's pouch and duodenal fistula. In this animal electrical irritation of the duodenum led to a depression of gastric secretion and diminution of its acidity, followed by destructive changes in the mucosa which ended in a fatal haemorrhage. The histological lesions were similar to those found in the guinea-pigs, rats, and rabbits.

Further proof that the formation of ulcers was a reflex phenomenon was provided by the fact that administration of barbiturates and ganglion-blocking drugs tended to prevent ulceration. *A. Swan*

1181. **Analytic Pathology. Histochemical Demonstration of Antibody Localization in Tissues, with Special Reference to the Antigenic Components of Kidney and Lung**

R. C. Mellors, M. Siegel, and D. Pressman. *Laboratory Investigation* [*Lab. Invest.*] **4**, 69–89, March–April, 1955. 23 figs., bibliography.

At the Sloan-Kettering Institute for Cancer Research, New York, the localization of antibodies and the antigenic components of tissues were studied *in vivo* in rats by the application of modern histochemical methods.

It was shown that rabbit antibodies against rat kidney and lung tissue were localized in the renal glomeruli of the rats, whereas antibodies against chicken ovalbumin were not so localized in the chicken's kidney. The main antigenic components of the kidney in these experiments were the glomeruli and their basement membranes. Localization of rabbit antibodies against rat lung was thought to occur in the pulmonary alveolar septa of the recipient rats and, as in the case of the antigenic components of the kidney, particularly in the basement membranes.

The significance of these findings in relation to the production of experimental glomerulonephritis is discussed. *J. B. Wilson*

1182. **Selective Renal Vasospasm and Ischemic Renal Necrosis Produced Experimentally with Staphylococcal Toxin. Observations on the Pathogenesis of Bilateral Cortical Necrosis**

A. Thal. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 233–259, March–April, 1955. 4 figs., 22 refs.

In experiments carried out at New York Hospital-Cornell Medical Center to obtain further information about the effect of bacterial toxins on the kidney, rabbits were given an intravenous injection of a standard amount of a filtrate of a culture of *Staphylococcus aureus* (Strain Wood 46). For the first 20 minutes following the injection the kidney showed no obvious change, but soon after that interval it began to swell and became intensely cyanotic. The renal vein went into spasm throughout its length, while the pulsation in the renal artery could no longer be seen. As judged by the results of intra-aortic or intravenous injection of indian ink, no blood was at this time entering the kidney. Between 40 and 120 minutes after the injection of toxin the renal blood flow had apparently completely ceased in nearly all the animals; between 3 and 6 hours afterwards it was partially or completely restored in many, and at the end of 2 days the renal circulation was normal in those

animals which survived. During the period of renal ischaemia the animals showed little general change except a transient oliguria, but about half the number died, at times varying from 9 to 36 hours after injection, with symmetrical necrosis of the kidney, although the renal circulation was then normal. The renal necrosis varied in extent, but commonly the entire cortex and most of the medulla were involved; the pelvic epithelium, pyramid, and many collecting tubules were usually spared. The changes, whether vascular or necrotic, were limited to the kidneys; they were not produced by filtrate heated to 60° or 80° C. for one hour or by filtrate mixed with an equal volume of staphylococcal antitoxin.

The author concludes that the renal vessels are particularly sensitive to staphylococcal toxin, that the renal necrosis produced is due to transient spasm of the renal vessels, and that the distribution of the renal necrosis depends on the degree and extent of the vasospasm.

C. L. Oakley

HAEMATOLOGY

1183. **An Improved Technique for Staining Blood Films with Giemsa Stain**

P. G. SHUTE. *Nature* [*Nature (Lond.)*] **175**, 727, April 23, 1955.

It has been found at the Medical Research Council Malaria Reference Laboratory, Horton Hospital, Epsom, that, in examining thick blood films for malaria parasites, if normal saline is used instead of distilled water to dilute Giemsa's stain and the films are immersed in the solution for 30 minutes, the erythrocyte envelopes of uninfected cells disappear, probably because the globulin is dissolved out by saline (but not by water). On the other hand the cells containing parasites become prominent, and in *Plasmodium vivax* infections Schüffner's stippling is sharply stained, thus facilitating species diagnosis.

Marjorie Le Vay

1184. **Stainable Ferric Iron Particles in Erythroid Marrow Cells and Erythrocytes**

W. I. MORSE. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **72**, 418–426, March 15, 1955. 2 figs., 17 refs.

To estimate the frequency with which stainable ferric iron particles occur in normoblasts and erythrocytes in different haematological conditions 68 patients were studied at Dalhousie University, Halifax, Nova Scotia. Smears of sternal marrow and blood films stained by the Prussian-blue method were examined and body storage iron and serum iron levels estimated.

The proportion of affected normoblasts was found to be low in chronic hypochromic anaemia, but high in pernicious anaemia and related megaloblastic anaemias, thalassaemia, and idiopathic erythraemic myelosis. The largest number of affected erythrocytes was observed after splenectomy in patients with a large proportion of affected normoblasts in the marrow, suggesting that the intracellular iron particles of erythrocytes were deposited in their precursors and that the intact spleen selectively removed affected erythrocytes from the circulation. In hypochromic anaemia the paucity of affected cells is regarded as an indication of more than average economy in the utilization of iron by erythroid marrow cells.

P. I. Reed

1185. **The Effect of Glass upon the Activity of the Various Plasma Clotting Factors**

S. I. RAPAPORT, K. AAS, and P. A. OWREN. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 9–19, Jan., 1955. 1 fig., 31 refs.

The initiation of blood clotting on the transfer of blood from contact with the vascular endothelium to a foreign surface such as glass is probably mediated not only through disruption of the platelets, but also by the activation of certain of the plasma coagulation factors. In the present study of the effect of glass on these coagulation factors, which was carried out at the University Hospital, Oslo, blood was collected in a silicone-coated vessel and the plasma largely freed of platelets by high-speed centrifugation at low temperature. Part of the plasma was left in the original vessel while part was shaken up with quartz glass powder and the two specimens were then tested separately for activity of the following coagulation components: antihaemophilic globulin (antihaemophilic A factor), Christmas factor (antihaemophilic B factor), prothrombin, Factor VII (proconvertin), and Factor V (proaccelerin). The activity of antihaemophilic globulin and of the Christmas factor was assayed by the ability to correct the calcium clotting times of plasma from patients deficient in these factors, while tests for prothrombin and Factors V and VII were made in one-stage systems, using brain tissue, in which there was an excess of all factors apart from the one being tested.

It was shown that the exposure to glass increased the activity of the Christmas factor and of Factor VII, but such exposure had no effect on the antihaemophilic-globulin activity, the prothrombin value, or Factor V. An observation of possible practical significance was that moderate reductions in the plasma content of Factor VII as a result of the administration of dicoumarol were masked by the activating effect of glass. The administration of heparin prevented the activation of Factor VII by glass.

A. S. Douglas

1186. **The Fibrinogen Polymerization Test in Active Rheumatic Disease**

S. LOSNER and B. W. VOLK. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 371–378, April, 1955. 1 fig., 24 refs.

After the administration of a therapeutic dose of heparin *in vivo* or the addition of a minute quantity to a blood sample *in vitro* the authors have observed that considerable amounts of fibrinogen remain in the serum separating after gross coagulation has taken place. They have therefore concluded that heparin interferes with the polymerization of fibrin, and in a study carried out at the Jewish Chronic Disease Hospital, Brooklyn, New York, have utilized this property in the investigation of the possible presence of polymerization accele-

rators in the serum in various diseases. The method is described in detail. Blood is drawn one hour after the intravenous injection of 50 mg. of heparin (or the heparin is added *in vitro*, 8 μg. to 3 ml. of blood) and clotted at 37° C. in 4 tubes in aliquots of 3 ml. each, 0·3 ml. of 0·1 M sodium citrate being added to the clotted blood at hourly intervals and the clot centrifuged down immediately. The supernatant serum is then investigated for the presence of fibrin, using the photoelectric prothrombin-time method, and the fibrinogen concentration is measured by determination of the density of the clot.

These tests were performed on the serum of 12 normal persons and of a number of patients with rheumatoid arthritis, rheumatic fever, and a variety of other clinical conditions, a total of 36 tests *in vivo* and 54 *in vitro* being carried out. A positive result was indicated by a complete consumption of fibrinogen. The results were negative in normal subjects, but were positive in active rheumatoid arthritis (22 cases) and active rheumatic fever (5 cases). Moreover, these test results remained positive long after laboratory criteria of the activity of rheumatic fever had returned to normal and they were not affected by the administration of cortisone. In the tests on serum from patients with such other diseases as glomerulonephritis, lupus erythematosus, or carcinomatosis the results were negative. The mode of action of heparin is discussed. It is concluded that heparin, in addition to its anticoagulant properties, can delay the polymerization of fibrinogen, and that this action is accelerated in the serum of patients with active rheumatic disease. *E. G. L. Bywaters*

1187. **Simultaneous ABO and Rh Groupings on Cards in the Laboratory or at the Bedside**
K. Eldon. *Danish Medical Bulletin* [*Dan. med. Bull.*] 2, 33–40, March, 1955. 9 figs., 19 refs.

The author describes a rapid method of ABO and Rh (D) blood grouping by means of pre-treated cards and without the need for specialized apparatus, which he devised and which has been in use at the blood bank at Kommunehospitalet, Copenhagen, since the beginning of 1951. The cards are coated with a film of regenerated cellulose (" cellophane ") on which are dried samples of anti-A, anti-B, anti-D, and inert serum, each in a separate panel. (The card is illustrated.) The grouping sera are selected for avidity and are mixed with suitable quantities of dextran, sodium chloride, and heparin before being placed on the card to dry, these additives enabling the reactions with whole blood to occur at room temperature (about 20° C.) without rouleaux formation and giving large clot-free masses of agglutination which can easily be read.

The grouping is performed by dissolving the dried test sera in water, after which a drop of the patient's capillary blood is added to each panel and stirred. The card is rocked and the reactions are read after 3 minutes. The testing of the subject's blood against inert serum detects auto-agglutination and indicates when the technique is not suitable for determining a particular patient's group, as, for example, in cases of acquired haemolytic anaemia. The results obtained may be covered with cellulose tape and permanently filed, particulars of the patient being added in the spaces provided on the card. Great accuracy is claimed for this quick bed-side grouping technique, only 6 cases of error having been found in 15,000 tests in which the results were checked by back-typing.

I. Dunsford

1188. **Blood Grouping in a Blood Bank by the Eldon Method**
K. Jordal. *Danish Medical Bulletin* [*Dan. med. Bull.*] 2, 40–44, March, 1955. 3 figs.

The author reports his experience with the Eldon card method of blood grouping (see Abstract 1187) at Kommunehospitalet, Copenhagen. He confirms that the method is simple, accurate, and speedy, and points out that its use in emergency reduces the likelihood of error and also of wastage of Rh-negative blood.

I. Dunsford

CHEMICAL PATHOLOGY

1189. **Cerebrospinal Fluid Inorganic Phosphorus in Acute Poliomyelitis. Study of One Hundred Four Patients**
L. Odessky, P. Rosenblatt, I. J. Sands, I. Schiff, F. M. Dubin, D. Spielsinger, J. A. Riesenberg, and L. Landau. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] 73, 255–266, March, 1955. 1 fig., bibliography.

The inorganic phosphorus concentration of the cerebrospinal fluid (C.S.F.) during the acute stage of poliomyelitis was studied in 110 specimens taken from 104 patients selected at random from 235 with poliomyelitis at the Kingston Avenue Hospital, Brooklyn, New York, during the epidemic of 1952. The cell count and total protein, globulin, and sugar concentrations were also determined for each specimen. The inorganic phosphorus levels in the C.S.F. ranged from 1·1 to 3·1 mg. per 100 ml., the mean value being 1·9 mg. per 100 ml. with a standard error of ±0·36 mg. per 100 ml. The difference between this value and the mean inorganic phosphorus content of C.S.F. from healthy subjects was statistically highly significant, the former being 36% higher than the latter.

There was no correlation between the C.S.F. inorganic phosphorus level and the age of the patient. In 91 of the specimens there were 10 or more cells per c.mm., lymphocytes accounting for at least half the total in approximately 70% of the specimens, polymorphonuclear leucocytes predominating in the remainder. In 68 specimens the total protein content was more than 45 mg. per 100 ml. and 71 specimens gave a positive reaction for globulin. The sugar content for all the specimens ranged from 61 to 98 mg. per 100 ml. The increase in the inorganic phosphorus level appeared to be a late manifestation of the disease, since the relative number of values " above the mean of 1·9 mg. per 100 ml. increased as the cytology of the C.S.F. changed from polymorphonuclear leucocytes to lymphocytes ".

However, it was not possible to relate the rise in the inorganic phosphorus level to the time elapsing since the onset of the disease.

The authors conclude that although pleocytosis in the C.S.F. remains the best indication of central nervous system involvement in poliomyelitis, the inorganic phosphorus level is of corroborative and, in some cases, of diagnostic value; in 9 cases in this series (one of bulbar poliomyelitis and 8 of non-paralytic poliomyelitis) an increase in the inorganic phosphorus level was the only abnormal finding in the C.S.F. They also suggest that phosphorus should be readily available for the treatment of patients in the acute phase of the disease.

M. J. H. Smith

1190. **Ammonia Levels in Blood and Cerebrospinal Fluid**
W. V. McDERMOTT, R. D. ADAMS, and A. G. RIDDELL. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **88**, 380–383, March, 1955. 1 fig., 15 refs.

In this paper from Harvard Medical School and the Massachusetts General Hospital, Boston, is described an investigation of the blood and cerebrospinal fluid (C.S.F.) levels of ammonia in 14 patients undergoing operation for portal hypertension or under observation or treatment for known liver disease, patients without liver disease subjected to operation under spinal analgesia serving as controls. Blood and C.S.F. were obtained simultaneously in all cases, the ammonia levels being determined by a modification of the microdiffusion method of Conway, which eliminates errors due to liberation of ammonia from glutathione.

In patients without liver disease ammonia content of the blood ranged from 51 to 65 μg. per 100 ml. and that of the C.S.F. from 2·7 to 14·7 μg. per 100 ml. The authors consider that the very small amounts of ammonia in the C.S.F. were probably due to contamination with tissue fluids. In all but one of the 14 patients with liver disease the ammonia concentrations of the blood and of the C.S.F. were raised, though the values for the C.S.F. were consistently lower than those for the peripheral blood. There was, however, a definite correlation between the two values. In all 5 patients in whom the ammonia concentration in the C.S.F. was greater than 105 μg. per 100 ml. there were significant disturbances of the central nervous system; the highest value recorded was 213 μg. per 100 ml., with a blood concentration of 326 μg. per 100 ml.

W. H. Horner Andrews

1191. **Trial Application of Nagler's Reaction in the Serological Diagnosis of Atherosclerosis in Man.** (Tentativo di applicazione della reazione di Nagler alla diagnostica sierologica della malattia aterosclerotica umana)
A. SCANU and S. SCHIANO. *Acta gerontologica* [*Acta gerontol.* (*Milano*)] **4**, 179–187, Nov.–Dec., 1955. 2 figs., 9 refs.

In 1938 Nagler (*Brit. J. exp. Path.*, 1938, **25**, 473) observed that when *Clostridium welchii* was grown in human serum opalescence developed and later a layer of fat rose to the surface. Subsequent investigations have shown that the alpha toxin of *Cl. welchii* is a highly specific lecithinase and the appearance of opalescence is a result of the breakdown of lipoprotein complexes after cessation of the stabilizing effect of lecithin in the serum. After purification of the lipoprotein fractions Peterman showed (*J. biol. Chem.*, 1946, **162**, 37) that maximum turbidity occurred in the β_1 lipoproteins and that the opalescence was negligible in the α-lipoproteins and in the other β-lipoprotein fractions. Considerable evidence has now accumulated which suggests that atherosclerosis in men and animals is connected with an increase in the β-lipoprotein content of the serum, and particularly of the β_1 fraction.

The present authors previously showed (*Riv. Ist. Sier. ital.*, 1954, **28**, 457) that for the production of Nagler's turbidity reaction a 5% watery solution of phenol can replace the alpha toxin of *Cl. welchii* and that this modification simplifies the method very considerably. At the Institute of Special Pathology, University of Naples, they therefore investigated the serum of 10 normal subjects, 20 atherosclerotic patients, 13 hypertensive patients, one with essential hyperlipaemia, and 2 cases each of nephrosis, liver cirrhosis, myeloma, and collagen disease. They found that all 20 atherosclerotic patients as well as the patients suffering from nephrosis and essential hyperlipaemia showed a strongly increased turbidity, whereas in none of the other cases were the normal limits of turbidity exceeded.

[The quantitative estimation of lipoprotein fractions is still a complicated procedure requiring special laboratory equipment and great experience. The described simplification of the method, which is much quicker than the original method using the alpha toxin of *Cl. welchii*, may prove therefore to be of considerable importance in the future.] *Z. A. Leitner*

1192. **Human Plasma Lipoproteins. I. In Normal Women and in Women with Advanced Carcinoma of the Breast**
M. BARCLAY, G. E. COGIN, G. C. ESCHER, R. J. KAUFMAN, E. D. KIDDER, and M. L. PETERMANN. *Cancer* [*Cancer* (*N.Y.*)] **8**, 253–260, March–April, 1955. 3 figs., 25 refs.

In a study of the effect of carcinoma on plasma lipoprotein levels carried out at Cornell University Medical College, New York, results obtained in 20 cases of carcinoma of the breast in women aged 30 to 49 (average 41) years were compared with those in 14 healthy women aged 30 to 45 (average 39) years. Of the patients with carcinoma, 5 had inoperable growths, while the other 15 had had radical mastectomy 3 months to 10 years previously. All 20 patients had metastases. All except one of the subjects, patients and controls, were still menstruating and therefore presumed to have minimal atherosclerosis; none had received hormone therapy, in none was there any evidence of thyroid or liver dysfunction, and all were receiving a normal diet. Thus other factors influencing lipoprotein metabolism were minimal.

Venous blood was taken in the morning before any fat-containing food was eaten, 50 ml. being collected over acid citrate dextrose in the cold, while 5 ml. was

heparinized. The plasma to which acid citrate dextrose was added was subjected to Cohn fractionation with ethanol at −5° C. The beta-lipoprotein precipitate was separated into low-density and high-density fractions (less than and more than 1·064 respectively) by the Gofman ultracentrifuge technique.

The mean cholesterol content of whole plasma was similar in the control subjects and the patients with carcinoma. In the former 27% of the total cholesterol was found in the alpha fraction, compared with 21% in the latter. The proportional amounts of cholesterol in the two subfractions of beta lipoprotein were identical in the two groups.

The mean phospholipid content of whole plasma was also similar in the two groups. As with cholesterol, the mean phospholipid concentration in the alpha fraction was lower in the patients, being about two-thirds the normal value. In the control subjects the percentages of phospholipids found in the alpha and beta fractions were approximately equal, while in the patients 37% was found in the alpha and 59% in the beta fraction. The distribution in the two subfractions of beta lipoprotein was similar in the two groups.

No significant difference was found in the levels of Sf_{2-10} components as between the controls and the patients. Significantly greater concentrations of the Sf_{11-20} and Sf_{21-100} components were found in the low-density beta fraction from the patients. The mean value for the Sf_{11-20} components was 55% higher for the patients than the controls, and the level of Sf_{21-100} components was 80% higher. The finding of marked elevations in Sf_{11-20} and Sf_{21-100} lipoprotein levels, together with normal cholesterol levels in the total low-density beta fraction, may be explained by the small concentrations of these components relative to the concentrations of Sf_{2-10} lipoprotein and by the progressively larger amounts of neutral fat in components greater than Sf_{13}. Further experiments suggested that some of the excess of Sf_{11-100} components might be related to the presence of bony metastases.

That the lipoprotein concentration and distribution in the patients with carcinoma were more like those in postmenopausal women than in the control group, despite the fact that they were still menstruating, is regarded as an indication that endocrine factors might be concerned. *Robert de Mowbray*

1193. Tubeless Gastric Analysis with an Azure A Ion-exchange Compound

H. L. Segal, L. L. Miller, and E. J. Plumb. *Gastroenterology* [*Gastroenterology*] **28**, 402–408, March, 1955. 2 figs., 11 refs.

The authors describe, from Rochester University School of Medicine, New York, the preparation of a cation-indicator compound containing azure A as the indicator-exchange ion and its use in a simple tubeless method of detecting free gastric hydrochloric acid, its presence being indicated by a blue–green colour change in the urine. The compound, which contained about 45 mg. of azure A per gramme of the carboxylic cation-exchange resin "amberlite XE 96", was prepared by dissolving a slight excess of azure A in water, adding the resin (conditioned in the hydrogen cycle), and stirring overnight; the exchange-indicator compound thus formed was filtered, washed by decantations with distilled water until no further dye was eluted, and dried at 50° C. for 2 days. By tests *in vivo* and *in vitro* the amounts of azure A (determined by spectrophotometer at a wavelength of 620 mμ) eluted from 1 g. of this compound in 30 minutes at 37·5° C. by dilute HCl, Ringer's solution, and distilled water were determined and are presented in a graph, which shows that the dye was displaced in significant amounts from solutions with a *p*H lower than 3, maximum displacement taking place at *p*H 1·5.

In a clinical test 2 g. of the azure-A compound in 100 ml. water was given orally to 127 subjects in whom the gastric secretory response had been previously determined by other methods. Urine was collected after 2 hours and the blue–green colour change in it was estimated colorimetrically. In 83 of the 85 known acid secretors the amount of azure A dye excreted averaged 1·6 mg. (range 0·66 to 3·91 mg.), while in 36 achlorhydric patients the average was 0·12 mg. (range 0 to 0·14 mg.). A border-line group of 4 patients showing low or intermittent acid secretion gave intermediate values. In the remaining 2 cases a cloudy or pigmented urine interfered with the determination of acidity by this method.

H. G. Crabtree

1194. Controlled Tubeless Test Meals

G. Behr and H. Lawrie. *Gastroenterology* [*Gastroenterology*] **28**, 409–411, March, 1955. 9 refs.

The "tubeless test meal" devised by Segal *et al.* (*Proc. Soc. exp. Biol.* (*N.Y.*), 1950, **74**, 218; *Abstracts of World Medicine*, 1950, **8**, 608) has become the accepted method of diagnosing achlorhydria, and the technique has been still further simplified by the introduction of the commercial resin "diagnex". Errors may occur, however, owing to (1) a false high quinine excretion caused by the interference of drugs containing aluminium, calcium, barium, iron, or quinine itself, or (2) false low quinine excretion caused by deficient absorption or excretion of this substance.

Writing from the Central Pathological Laboratory, Burnley, Lancashire, the authors point out that errors due to the first cause may be avoided by stopping all therapy 48 hours before the test. Those of the second type can be detected by the introduction of a positive control test; in this, after the third specimen of urine has been collected, 36 mg. of quinine hydrochloride is given and analysis of the urine 2 hours later shows whether the patient can absorb and excrete quinine, false negative results being indicated if the excretion of quinine is less than 20 μg. in the specimen. This controlled technique was used in 97 cases, among which 8 possible mistaken results were detected. In a study of the urinary excretion of quinine by 8 patients with diminished renal function no correlation was found between the blood urea level or the presence of albuminuria and the ability to excrete quinine.

H. G. Crabtree

1195. **Serum Cholinesterase in Hepatic and Neoplastic Diseases: a Preliminary Report**
D. W. MOLANDER, M. M. FRIEDMAN, and J. S. LADUE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 1139–1151, Dec., 1954. 2 figs., 18 refs.

A new method of determining serum cholinesterase activity is described by which the acetic acid liberated by the esterase by hydrolysis of acetylcholine added to the serum in known amount and under controlled conditions is measured colorimetrically, with phenol red as indicator.

Serum cholinesterase levels have been determined in 20 patients with primary liver disease, including hepatitis, cirrhosis, and primary carcinoma of the liver, and in 37 cases in which the liver was involved as a complication of a primary disease located in some other organ. The latter group included patients with metastatic carcinoma or lymphoma and some with obstructive jaundice. In general, low values were found in acute parenchymatous liver disease and in metastatic carcinoma and lymphoma complicated by spread to the liver, and varying values in chronic disease of the liver. It is concluded that serum cholinesterase levels may provide confirmatory evidence of parenchymal liver damage, and may at times be the only evidence of such dysfunction in patients with metastatic carcinoma and lymphoma of the liver.

L. A. Elson

1196. **Creatinine Clearance and Thiosulphate Clearance as Tests of Renal Function.** (La comparaison entre la créatinine clearance et hyposulfite clearance comme procédé d'exploration fonctionnelle du rein)
A. AMERIO, A. VERCELLONE, and G. LUNEL. *Presse médicale* [*Presse méd.*] **63**, 572–573, April 20, 1955. 1 fig., 23 refs.

The authors comment on the inconsistent results obtained by many workers when comparing the renal clearance of creatinine with that of other substances such as inulin, mannitol, and sodium thiosulphate, and in this study carried out at the Institute of Pathology, University of Turin, have attempted to explain these inconsistencies. Resting endogenous creatinine clearance tests were first carried out on 20 normal subjects and on 53 patients with acute or chronic glomerulonephritis in different stages of the disease, after which continuous intravenous sodium thiosulphate was administered. The clearance of creatinine was then again determined, as well as the thiosulphate clearance.

In normal subjects the results of simultaneous thiosulphate and creatinine clearance tests were approximately equal. On the other hand the ratio of thiosulphate clearance to resting creatinine clearance exceeded unity consistently and significantly. In patients with acute glomerulonephritis the thiosulphate clearance was reduced to about one-third of its normal value, while the ratio of thiosulphate clearance to resting creatinine clearance fell towards unity. In those with chronic glomerulonephritis this ratio remained approximately at unity during the stage of relative tubular insufficiency, but fell below unity during the stage of absolute tubular insufficiency.

The authors tentatively conclude that, whereas resting creatinine clearance indicates the functional glomerular activity in the absence of any exogenous stimulus, thiosulphate clearance indicates functional glomerular activity after stimulation by exogenous thiosulphate. They suggest that the thiosulphate stimulates resting glomeruli into action, thus causing in the normal subject an increased glomerular filtration rate and hence, as a consequence of the increased rate of flow of pre-urine along the tubules, diminished tubular reabsorption. Thus, a ratio of thiosulphate clearance to resting creatinine clearance significantly greater than unity is an indication of glomerular functional reserve. When this ratio approaches unity, glomerular functional reserve is approaching zero, while a fall in this ratio to less than unity indicates that not only has glomerular functional reserve been lost, but also that the renal tubular epithelium has lost some or all of its ability to act as a barrier against the test substance. *Adrian V. Adams*

MORBID ANATOMY AND CYTOLOGY

1197. **Cytology and Cellular Pathology of the Oligodendrogliomas of the Brain**
J. R. RAVENS, L. L. ADAMKIEWICZ, and R. GROFF. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **14**, 142–184, April, 1955. 48 figs., bibliography.

Despite improvements in staining technique permitting differentiation of the various types of cell and other characteristics of cerebral oligodendrogliomata, a certain amount of overlapping and confusion still exists in the classification of these tumours. To elucidate the problem the authors have made a histological study of material removed from 39 patients with oligodendroglioma at the Graduate Hospital of the University of Pennsylvania, Philadelphia. They found that these neoplasms are characterized by small cells with spherical nuclei and scanty cytoplasm, the cells appearing rounded, angular, polygonal, or pyriform, with scanty cytoplasmic extensions. They were able to recognize 5 types of oligodendroglioma—diffuse, pseudo-alveolar, loose, lacunar, and alveolar—each of which presented a characteristic appearance; but they consider that there is only one principal type, the diffuse, the others being subtypes.

These tumours generally exhibited an interesting pattern of blood-vessel arrangement and a scarcity of connective tissue. Nerve cells in the central part of the tumour showed acute degeneration, while more peripherally changes in the nerve cells varied in degree. Almost invariably hypertrophy of the remaining astroglia was observed. The microglia also exhibited nucleocytoplasmic changes, usually resulting in hypertrophy. Some neoplastic oligodendrocytes showed evidence of transition to more mature differentiation. Of the 39 specimens examined, 9 appeared to be oligodendrogliomata in transition. There were two trends: tumours near the surface of the brain tended to develop into protoplasmic astrocytomata, while those deep in the white matter had a tendency to develop into the fibrillary

astrocytic forms. Some tumour cells became astroblasts with malignant potentiality.

Clinical features noted were that these tumours arose in early middle life, had a longer course of symptoms than other types of glioma, and usually recurred in the cerebral hemisphere. The deeper tumours ran a more rapid course than the cortical ones with regard to the development of signs and symptoms. The common clinical picture was that of headache and rising intracranial pressure; motor disturbances were frequent and radiological evidence of intracranial calcification was common. Of the 39 patients concerned in this investigation, 10 survived 5 years. *J. V. Crawford*

1198. **The Adenohypophysis and Hypothalamus in Hyperadrenalcorticalism**
L. W. O'Neal and P. Heinbecker. *Annals of Surgery* [*Ann. Surg.*] **141**, 1–9, Jan., 1955. 7 figs., 28 refs.

The authors, writing from Washington University and Barnes Hospital, St. Louis, Missouri, discuss the pathogenesis of Cushing's syndrome in the light of the histological findings on examination of the hypothalamus and of serial sections of the pituitary glands from 2 fatal cases of Cushing's syndrome, 9 cases in which death followed prolonged cortisone therapy for various conditions, and 3 control cases. In the cases in which prolonged cortisone treatment had been given the number of basophil cells in the pituitary glands was high, but the proportion of hyalinized basophil cells (Crooke's cells) present was inconstant. It is suggested, therefore, that Crooke's cells are secondary to the hyperadrenocorticalism and do not play a primary role in the pathogenesis of Cushing's syndrome. Further, the lack of any abnormality in the hypothalamus in some of these cases suggests that degenerative changes in the paraventricular nuclei cannot be the only factor in the pathogenesis of the syndrome. *B. Nordin*

1199. **Histoplasmosis of the Central Nervous System**
J. L. Shapiro, J. J. Lux, and B. E. Sprofkin. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 319–335, March–April, 1955. 11 figs., 12 refs.

The frequency with which histoplasmosis affects the central nervous system is not generally recognized. A review of the necropsy records of 23 cases of this disease at the Vanderbilt University Hospital, Nashville, Tennessee, showed that there was cerebral involvement in 6 of the 11 cases in which the brain was examined; in 2 of the cases there were also marked neurological symptoms. Clinical details of the 6 cases together with the post-mortem findings are presented.

In their discussion the authors describe the disease as resembling tuberculosis, the lesions occurring in the brain, meninges, and choroid plexus being individually about the same size as the miliary tubercle. In the lungs occur small lesions which calcify or larger lesions which may cavitate. Microscopically, however, the histiocytes contain the characteristic yeasts, and giant cells are common.

In the central nervous system 3 types of histoplasmosis occur: (1) scattered "tubercles" forming part of a generalized dissemination; (2) the "histoplasmoma", a larger type of lesion usually associated with similar progressive lesions in the viscera; and (3) a generalized meningitis with exudation of polymorphonuclear granulocytes accompanying fibrinoid necrosis of the arterial walls as well as a focal lesion. It is pointed out that although involvement of the central nervous system is secondary to histoplasmosis elsewhere, the initial focus may be small and thus overlooked. *D. M. Pryce*

1200. **A Contribution to the Histology and Pathogenesis of Tabes Dorsalis.** (Contributo all'istopatologia e patogenesi della tabe)
V. Floris and A. Pansini. *Rivista di neurologia* [*Riv. Neurol.*] **25**, 1–18, Jan.–Feb., 1955. 17 figs., 22 refs.

At the University Clinic for Nervous Diseases, Padua, the authors have examined in some detail the histological features of the spinal cord, spinal nerve roots, and meninges in 6 cases of tabes dorsalis. On their findings, which are described, they base the hypothesis that the infection first attacks epidural structures, and thence proceeds to affect the meninges and finally the cord itself. The paper is illustrated by a number of clear photomicrographs. *L. Michaelis*

1201. **Atypical Adenoma of the Thyroid**
J. B. Hazard and R. Kenyon. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **58**, 554–563, Dec., 1954. 8 figs., 8 refs.

Out of a series of 2,452 thyroid adenomata (all solitary, encapsulated, non-papillary nodules resected at the Cleveland Clinic, Ohio) the authors found 57 "atypical" tumours with close-packed epithelium suggestive of malignancy. A study of nuclear atypicality and the frequency of mitosis revealed no difference between this group of tumours and the angio-invasive group described previously by the authors (*Amer. J. clin. Path.*, 1954, **24**, 755; *Abstracts of World Medicine*, 1955, **17**, 88), but whereas metastases were frequently observed in the earlier series (in at least 15 out of 32 cases) no evidence of malignancy was found in the present series. [The authors' investigation resolves itself into a simple demonstration that vascular invasion is the only reliable evidence of malignancy in encapsulated thyroid adenomata.] *Bernard Lennox*

1202. **The Histology of Cancer of the Thyroid**
W. W. Park and J. C. Lees. *Cancer* [*Cancer* (*N.Y.*)] **8**, 320–335, March–April, 1955. 20 figs., 13 refs.

The authors, in an attempt to define the criteria for diagnosis of malignancy in tumours of the thyroid by relating histology to clinical behaviour, reviewed 66 cases diagnosed histologically during a 20-year period at the Royal College of Physicians' Laboratory at Edinburgh. They divided their material into 3 groups. The first group consisted of 36 unequivocally malignant neoplasms, 25 of which were regarded as undifferentiated carcinomata, 2 as epidermoid carcinomata, 2 as solid alveolar carcinomata, 1 as eosinophil-cell carcinoma, 1 as mucoid carcinoma, 3 as sarcomata, and 2 as lymphosarcomata. This group carried a very poor prognosis,

only 2 of the patients being known to be alive 13 and 6 years respectively after operation; both tumours were diagnosed as undifferentiated carcinoma. The second group contained 15 cases of papillary neoplasm. Of these, 9 were originally reported as papillary adenoma; 5 of the patients could be followed up and were alive and well from 3 to 18 years after operation. In 6 cases the growth was originally regarded as papillary adenocarcinoma; 4 of the patients had died from a variety of causes, and 2 were alive and well 6 years after the tumour was excised. The original diagnosis of malignancy was rejected in 8 of the 15 cases in the third group, and this view was supported by the clinical outcome. The remaining 7 cases were classed as of doubtful malignancy, and only one patient was known to have died with generalized metastases, 6 months after operation. The authors did not encounter cancers of microscopic dimensions, and consider invasion of the blood vessels to be of little value as a criterion of malignancy. They recommend that undifferentiated and papillomatous growths, as well as Hürthle-cell tumours, should for practical purposes be regarded as malignant; they also discuss the features of epithelial hyperplasia associated with lymphatic hyperplasia, most cases of which they regard as benign. *R. Salm*

1203. **The Pathology of Non-specific Oesophagitis**
K. V. LODGE. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **69**, 17–24, 1955. 9 figs., 26 refs.

The macroscopical and histological appearances of the oesophagus at necropsy on 500 unselected hospital patients and 100 who died suddenly from accident or illness of less than 24 hours' duration are discussed in this paper from Manchester University. Evidence of oesophagitis was found in 180 (36%) of the hospital patients—acute oesophagitis in 155 and chronic in 25—and in 8 of the subjects who died suddenly—acute in 3 and chronic in 5. The cases of acute oesophagitis were divided into three groups according to the degree of severity of the condition. In Group 1 (53 cases) there was inflammatory infiltration without ulceration; in Group 2 (67 cases) there was focal ulceration; and in Group 3 (38 cases) widespread ulceration of the epithelium with extension of the inflammatory reaction into the external muscle layer. A study of the possible relationship between the oesophagitis and the primary disease in the hospital patients revealed an association only in those suffering from diabetes mellitus, peritonitis, or pyogenic infections. The only associated biochemical abnormality was a reduced alkali reserve. The considerably higher incidence of oesophagitis in the hospital patients compared with patients dying suddenly suggested that confinement to bed played an important part, the principal aetiological factor in these cases being reflux of gastric contents into the oesophagus during continued vomiting, gastric intubation, and prolonged recumbency.

The clinical significance of non-specific oesophagitis is discussed, and it is suggested that stricture and shortening of the oesophagus are possible sequelae of the more severe acute lesions. *J. L. Markson*

1204. **Studies in Lung Structure by Low-voltage Radiography**
G. J. CUNNINGHAM. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 253–260, March, 1955. 9 figs., 12 refs.

The author describes, from St. Bartholomew's Hospital, London, a method of studying lung structure in health and disease by means of radiography with low-voltage or "soft" x rays. By this means pictures resembling those seen by the naked eye are obtained with the added advantage that a depth of tissue is viewed. The radiographs can also be taken stereoscopically and viewed through a stereoscope adapted for the purpose. They provide permanent records of the appearances of the lung [and some are very beautiful]. The best results are obtained when the specimen contains air. In densely fibrosed lungs only the outlines of the bronchi can be discerned. Lungs affected by emphysema, bronchiectasis, pneumoconiosis, infection, and tumour have been studied, but recently the investigation has been concentrated on coal-miner's lung. The appearances in all these conditions are described and illustrated.

D. M. Pryce

1205. **A Contribution to the Study of Tuberculosis of the Cartilaginous Bronchi.** (Contribution à l'étude de la tuberculose des bronches cartilagineuses)
P. GALY, R. G. TOURAINE, and A. MINETTE. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **19**, 26–37, 1955. 7 figs., 11 refs.

While it has generally been thought that tuberculous involvement of the little-known supralobular bronchi—which, like the bronchi proper and unlike the bronchioles, contain cartilage in their walls—is usually secondary to parenchymatous or adjacent lymph-node lesions, the authors report that examination of pathological material from tuberculous patients indicated that these supralobular divisions of the bronchi proper may constitute the centre of caseous, nodular tuberculous foci more frequently than has been thought, and are often involved in lesions which have hitherto been regarded as involving only the non-cartilaginous bronchioles. The ultimate supralobular divisions of the bronchi may be distinguished from the bronchioles by the presence of minute plates of cartilage and by a diameter exceeding 1 mm., the calibre of the accompanying artery being greater than that of the bronchiolar arteries.

The evidence collected suggests that the development of such lesions from the supralobular bronchi is centrifugal and therefore raises the question of a bronchogenic origin. *R. Crawford*

1206. **Chemically Identifiable Bacterial Residues in Lung Lesions**
R. CONSDEN and L. E. GLYNN. *Lancet* [*Lancet*] **1**, 943–945, May 7, 1955. 1 fig., 10 refs.

The authors, in view of their wide experience of the chemistry of subcutaneous rheumatic nodules undertook examination, at the Canadian Red Cross Memorial Hospital, Taplow, of various types of lung nodule on behalf of workers in South Wales studying the prob-

lems of pneumoconiosis. The lung tissue was treated to remove interfering substances, hydrolysed, and the resulting solution subjected to chromatography in one direction, followed by iontophoresis in a direction at right angles to this, the separated amino-acids being demonstrated with ninhydrin. [The original paper should be consulted for the technical details of these procedures.]

Samples of a caseous nodule, a nodule as described by Caplan (*Thorax*, 1953, **8**, 29), and a specimen of non-caseous tuberculous lung were all found to contain α-ε-diaminopimelic acid. This substance, which does not occur in normal mammalian tissue, is present in various bacteria, including *Mycobacterium tuberculosis*. None was found in a sample of pulmonary tissue showing progressive massive fibrosis, in an " infective nodule " of Gough, or in normal lung. Calculation showed that at least 2·5% of the dry weight of the lesions containing α-ε-diaminopimelic acid consisted of bacterial residue, while in the caseous nodule they constituted as much as 20% of the lesion.

The authors suggest that this technique of detecting bacterial debris by demonstrating the presence of chemically characteristic components may be useful in investigating diseases of obscure aetiology, such as sarcoidosis. *M. C. Berenbaum*

1207. **Cytologic Diagnosis in Suspected Pulmonary Cancer. Critical Analysis of Smears from 100 Persons**
N. C. Foot. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 223–240, March, 1955. 18 figs., 6 refs.

To evaluate the film method of diagnosis of pulmonary cancer the author has studied the reports of cytological examination of smears of sputum and/or bronchial aspirates or washings in 1,000 cases in the files of the Cornell University Laboratory of Experimental Cytology out of more than 7,000 cases dealt with during the last 10 years. He examined the slides himself and compared his results with those obtained by the laboratory.

The study has shown that diagnosis is not dependent on delicate shades of difference in the appearance of smears. Usually in a positive case the tumour—even the tiniest intra-epithelial carcinoma—exfoliates copiously, and long before it is visible by radiological examination. " It is," the author states; " the doubtful cases, in which a few atypical cells are detected, that give rise to speculation (rather than definite diagnosis) and to false-positive reports." [But the number of false positive reports is nonetheless alarming. Discarding these cases in which the cytological diagnosis could not be subsequently checked by other means, 16 of 162 positive reports by the author (about 10%) were wrong. The laboratory was much more successful: only 4 wrong (about 3%) out of 137 positive reports.] The author considers that experienced technicians are often able to make a diagnosis of pulmonary neoplasm, but that it would be unethical, and even illegal, for them to do anything more than screening. [But obviously from his figures even the opinion of the medically qualified should not be accepted without question.] *D. M. Pryce*

1208. **Pulmonary Lesions in Disseminated Lupus Erythematosus**
D. C. Purnell, A. H. Baggenstoss, and A. M. Olsen. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 619–628, March, 1955. 3 figs., 13 refs.

The gross and histological lesions in the lungs of 54 patients dying from disseminated lupus erythematosus are described in this paper from the Mayo Clinic. Secondary infection and evidence of vascular damage were found in most of the cases. No actual lesions such as " fibrinoid degeneration " were observed in the vessel walls, but in 9 cases there was a curious mucinous oedema in the perivascular and peribronchial tissues with some spread into the alveolar walls. It is suggested that this may be the precursor of fibrinoid change.
A. C. Lendrum

1209. **Uremic Pneumonitis**
H. C. Hopps and R. W. Wissler. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 261–273, March–April, 1955. 6 figs., 6 refs.

The lesions in uraemic pneumonitis are more familiar to radiologists than to pathologists, who tend to overlook the condition because the changes are not specific. Microscopical examination of the lungs in uraemic pneumonitis reveals moderate oedema, usually rich in protein, and a considerable amount of fibrin in the alveoli. The latter is seen as a fine network, occasionally in dense hyaline masses, and sometimes as an asphyxial membrane. Macrophages are observed in most cases. The diffuse pulmonary lesions most closely resemble those of rheumatic pneumonitis but in the latter condition vascular necrosis may be seen.

At the University of Chicago examination of the necropsy records covering a period of 40 years revealed 107 cases of uraemia; in 66 there was uraemic pneumonitis. The incidence of the condition was highest in patients with a blood urea nitrogen level of 60 mg. per 100 ml. A significant finding was that in all 8 cases in which the blood carbon dioxide combining power was below 10 mEq. per litre and in 24 out of 26 in which it was below 20 mEq. per litre uraemic pneumonitis was present.

In the authors' view the fact that uraemic pneumonitis appears to occur less frequently nowadays reflects the more effective control of the acid–base balance in the modern treatment of uraemia. *D. M. Pryce*

1210. **Primary Pulmonary Arterial Disease. Observations with Special Reference to Medial Thickening of Small Arteries and Arterioles**
F. Goodale and W. A. Thomas. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **58**, 568–575, Dec., 1954. 1 fig., 14 refs.

Only 2 cases of primary pulmonary hypertension without evident cause were found in 10,000 consecutive necropsies carried out at the Massachusetts General Hospital, Boston; the first patient, a boy of 6 months, had had cyanosis for 6 weeks only before death, while the second, a boy of 10 years, had had cyanosis for 2 years. In both cases there was marked muscular

hypertrophy of the pulmonary arterioles. Out of a number of control cases in which sections of the pulmonary vessels were examined (including 30 cases of mitral stenosis, 22 of congenital heart disease, and 9 of malignant systemic hypertension), similar arteriolar changes were seen in only 5 cases of congenital heart disease with left-to-right shunt. In the majority of cases of pulmonary hypertension, and in all those in which the condition developed after birth, there was intimal fibrous thickening in place of the medial hypertrophy. The authors draw attention to the relatively greater thickness of the media in the arterioles of the foetal lung and the high resistance of the pulmonary circulation in the foetus, and suggest that in their 2 cases there was persistence of the foetal state.

[Presumably the pulmonary veins were examined in these cases, though this is not mentioned. There has recently been a sharp reminder that anomalies of pulmonary veins are easy to miss even at necropsy, and that they can closely mimic the effects of primary pulmonary hypertension.] *Bernard Lennox*

1211. **Post-mortem Radiography of the Coronary Arteries in the Aged.** (La coronarographie post mortem de l'homme âgé)

P. P. VAN DER STRAETEN. *Acta cardiologica* [*Acta cardiol. (Brux.)*] **10**, 15–43, 1955. 7 figs., 39 refs.

The coronary circulation of 34 subjects ranging in age from 45 to 88 years, the mean age being 64·6 years for the males and 71·2 years for the females, was examined radiologically post mortem at the Civil Hospital, Ixelles, Belgium. After a plain radiograph had been taken both coronary arteries were catheterized and into the right artery was injected 1 to 3 ml. of 40% heavy iodized oil; a second radiograph was then taken. Lastly, a third radiograph was obtained after the left coronary artery had been injected with 2 to 5 ml. of the contrast medium.

Two distinct and independent types of pathological change were observed. (1) The first consisted in tortuosity of the vessels, which was observed in all cases and became more marked with increasing age. This is interpreted as an expression of the lengthening and extension of the vessels following the loss of elasticity due to degeneration of the longitudinal muscle fibres of the arterial wall. It affected only the arteries of medium and small calibre and was more marked in those of muscular type than in those of elastic type; it was not necessarily associated with cardiac ischaemia. (2) The second type of change was manifested by localized or extensive plaques of atheroma which narrowed the lumen of the coronary trunks, often giving a beaded appearance on the radiograph; in some cases calcification in the wall of the vessel gave rise to the appearance of a double contour. This second type of change was found less constantly than the first and bore no relation to it in severity, although the frequency and importance of both types of lesion tended to increase with age. In the second type, in contrast to the first, it was the larger coronary trunks which were most commonly affected and the smallest branches not at all. In some cases the flow of opaque medium was seen to be obstructed by a thrombus, an embolus, or an atheromatous plaque; in such cases anastomoses were observed between the collateral vessels. *Robert de Mowbray*

1212. **Myocardial Lesions of Early Childhood.** [In English]

E. K. AHVENAINEN and L. HJELT. *Annales paediatriae fenniae* [*Ann. Paediat. Fenn.*] **1**, 12–26, 1954–55. 6 figs., 14 refs.

The incidence of myocardial lesions in childhood was studied at the Children's Clinic, Helsinki, in specimens of heart muscle taken at necropsy on 595 children who died under the age of one year during the period 1950 to 1952. By a combination of macroscopical and microscopical examination myocardial lesions were found in 14 (2·3%) of the cases. Four types of lesion were seen. (1) Metastatic lesions from evident infections elsewhere (7 cases), the infecting organism being *Pseudomonas aeruginosa* (3 cases), *Staphylococcus aureus* (2), *Candida* sp. (one case), and an unidentified Gram-negative bacillus (one). The lesions were, in the main, pericarditis with myocardial extension, focal myocardial abscess, or endocardial abscess. (2) Apparently infective myocardial lesions without obvious infections elsewhere (5 cases). In 4 cases there was diffuse and focal granulocytic infiltration and in the fifth case inclusion disease with myocardial lesions. (3) Foetal endomyocardial fibroelastosis (2 cases). (4) Muscular lesions (5 cases). Calcinosis was present in one of these, while in 4 there was abnormal staining, associated in 2 cases with kernicterus.

Commenting on the difficulty of recognizing symptoms of myocarditis the authors suggest that in diseases of children electrocardiography should be carried out more systematically than it is at present. *C. L. Oakley*

1213. **Pathology of Hemorrhagic Fever. A Comparison of the Findings—1951 and 1952**

A. STEER. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 201–221, March–April, 1955. 10 figs., 15 refs.

In 1951 a total of 876 cases of haemorrhagic fever, with a mortality of 6·4%, occurred among the U.S. Forces in Korea; in 1952 1,067 cases, with a mortality of 4·9%, were observed. The fall in mortality was not considered to be due to a decrease in severity of the disease (indeed, the cases seen in 1952 appeared clinically more serious than those seen in 1951), but to better treatment of the cases in a single centre with more experienced staff, and to restriction of fluid in the oliguric stage. Deaths in the oliguric stage were far fewer in 1952 than would have been expected from the 1951 experience, but deaths in the other stages agreed with expectation. The disease could be divided into fairly well defined clinical stages (fever, hypotension or shock, oliguria, diuresis, and recovery). Adequate post-mortem records and clinical information were available in 50 cases in 1952, compared with 61 in 1951.

In both years most deaths occurred on the 8th day of illness, with a rapid fall in the number of deaths on

either side of this time; occasional deaths occurred as late as the 32nd day. Delay in admission to hospital appeared to have little effect on the outcome. In the febrile stage death appeared to be due to a circulating toxic agent causing high fever, circulatory collapse, a leukaemoid blood reaction, haemorrhages, and severe shock; in the oliguric and diuretic stages death was due to renal failure, pulmonary oedema, pulmonary suppuration, or cerebral haemorrhage, or a combination of these. The kidneys often became involved in patients in whom shock was mild.

Weights of lungs, heart, spleen, kidney, and liver in fatal cases were consistently lower in the 1952 epidemic than they were in that of 1951, though there was little difference in the patients' body weights. Pulmonary oedema and pneumonia were rarer in 1952 than in 1951, but when pneumonia did occur it was often more severe. In 1952 the heart weight was normal at all stages of the disease; in 1951 it was increased at all stages. Though retroperitoneal oedema occurred with much the same degree of severity in both years, and seemed to bear little relation to the severity of shock, serous effusions were less severe in 1952 than in 1951.

Microscopic changes were found in all hearts, less constantly in the kidney and adrenal gland. Haemorrhage was always present in the right atrium; in addition there was irregular subendocardial infiltration, often perivascular, with plasma cells, Anitschkow's cells, mast cells, and eosinophil and occasional polymorphonuclear granulocytes, often extending for a short distance between muscle fibres. There was no change in the vessel walls, except occasionally beneath the endothelium of the aorta and coronary arteries, where there was infiltration with mononuclear leucocytes. No rickettsiae could be demonstrated in the infiltrating cells.

Ischaemic infarction occurred frequently in the kidney and pituitary, less frequently in the adrenal gland. The renal "haemorrhages" appear to be due not to extravasation of blood from ruptured vessels, but to stagnation of blood in dilated vessels and diapedesis of erythrocytes.

C. L. Oakley

1214. **The Pathogenesis of Fibrocystic Disease of the Pancreas. Study of the Ducts by Serial Sections**
R. A. ALLEN and A. H. BAGGENSTOSS. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 337–351, March–April, 1955. 20 figs., 25 refs.

Of the many theories which have been advanced in the past to explain the pathogenesis of fibrocystic disease of the pancreas the most widely supported include vitamin-A deficiency, imbalance of the sympathetic nervous system, altered secretion of the glands, including the pancreas, inflammation, and congenital malformation of the pancreatic ducts. At the Mayo Clinic 8 cases of fibrocystic disease were studied, serial sections being prepared of the head of the pancreas and papilla of Vater. Macroscopically the pancreas was normal, but serial sections revealed varying degrees of atresia of the ducts. In one case the ampulla was obliterated and in another it was stenosed. In all cases the interlobular and intralobular ducts were both affected.

D. M. Pryce

1215. **Polycystic Liver. Analysis of Seventy Cases**
P. J. MELNICK. *Archives of Pathology* [*Arch. Path. (Chicago)*] **59**, 162–172, Feb., 1955. 15 figs., 18 refs.

After reviewing the relevant literature the author gives an account of the findings at necropsy in 70 cases of polycystic disease of the liver seen over a period of 36 years at the Los Angeles County General Hospital. Only one case had been diagnosed in life, by means of peritoneoscopy.

The polycystic changes in the liver appeared to develop progressively over years. No case showed evidence of parenchymal involvement. Meyenburg's complexes (of small bile ducts in the lobules separate from the portal systems) were present in 29 cases. Some livers had multiple cysts, others only few, the cysts containing clear fluid. Bile ducts, gall-bladder, parenchyma, and hepatic blood vessels were all normal. There was a notable correlation between the presence of polycystic changes in the liver and cystic changes in the kidney and to a less extent in the pancreas; there was also some correlation with the existence of benign and malignant tumours elsewhere in the body. In 4 cases the polycystic liver was associated with polycystic kidneys and aneurysms of the cerebral arteries, and in 2 cases new formation of bile ducts from liver-cell cords was observed.

Details of representative cases are given.

B. G. Maegraith

1216. **Diffuse Intra-sinusoidal Metastatic Carcinoma of the Liver**
A. J. WATSON. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **69**, 207–217, 1955. 7 figs., 22 refs.

Out of a total of 279 cases of carcinoma coming to necropsy at the Welsh National School of Medicine, Cardiff, between January, 1951, and March, 1954, only 5 cases of diffuse intra-sinusoidal carcinomatosis of liver were discovered. The patients were males, aged 59, 59, 48, 45, and 40 respectively, and all had a primary bronchial neoplasm. Only 13 similar cases were found in the literature, and in none of these was the primary growth in the bronchus. The author states that there is no adequate explanation for the peculiar metastatic deposits. Clinically and post mortem the condition may be confused with leukaemia, amyloidosis, or diffuse fibrosis of the liver. Of particular interest is the relationship of this condition to factors controlling the survival and extravascular extension of tumour emboli, for which there is as yet no satisfactory explanation.

A. Wynn Williams

1217. **Asymmetrical Liver Disease in Infancy**
J. L. EMERY. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **69**, 219–224, 1955. 5 figs., 16 refs.

Asymmetrical liver disease was found in 4 out of 500 infants under the age of one year on whom necropsy was performed at the Children's Hospital, Sheffield. In all 4 cases degenerative, necrotic, atrophic, and fibrotic lesions were notably more severe in the left than in the right lobe of the liver. The author suggests that in 3 cases the condition was the result of neonatal infective hepatitis and in the fourth, in which there was severe and prolonged anoxia immediately after birth, it

was due to failure to establish an adequate circulation in the left lobe of the liver. He attributes the asymmetry of the changes in the first 3 to the effect of infection superimposed on the physiological involution of the left lobe of the liver which occurs immediately after birth.

A. Wynn Williams

1218. **Signet-ring Cell Carcinoma of the Urinary Bladder**
O. SAPHIR. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 223–231, March–April, 1955. 9 figs., 5 refs.

The author, from the Michael Reese Hospital, Chicago, describes and illustrates a case of carcinoma of the urinary bladder, misdiagnosed during life as carcinoma of the prostate, in which the predominant cell was distended with mucin to such an extent as to compress the nucleus. To this type of growth the name signet-ring-cell carcinoma has been given. Like other similar carcinomata previously reported, the growth infiltrated the bladder diffusely, with early involvement of the ureteric orifices and little projection into the bladder lumen. Death occurred in 4 months from uraemia; there were no metastases. The author considers that some signet-ring-cell carcinomata of the ovary or intestine may be metastatic from the bladder.

C. L. Oakley

1219. **Subcutaneous Pseudosarcomatous Fibromatosis (Fasciitis)**
B. E. KONWALER, L. KEASBEY, and L. KAPLAN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 241–252, March, 1955. 12 figs., 7 refs.

The authors describe under the name of subcutaneous pseudosarcomatous fibromatosis 8 cases of a lesion which many pathologists [including the abstracter] have diagnosed as sarcoma but which they suspect is innocent and possibly not a neoplasm at all. [Certainly the biopsy rate for sarcoma of the skin and deeper tissues is higher than results of necropsy would warrant.] Although histologically it resembles fibrosarcoma or even angiosarcoma, they consider it to be of the nature of an inflammatory reaction. Indeed, some of its histological features would suggest a relationship to the cutaneous conditions known as nodular subepidermal fibrosis, sclerosing angioma, and histiocytosis.

They deprecate the use of major surgery in these cases, but at the same time point out that removal of the lesion should not be ruled entirely by cosmetic considerations. A systematic 5-year follow-up of a number of cases is under way at the Memorial Hospital, New York.

D. M. Pryce

1220. **Degenerative Lesions of Tendinous and Aponeurotic Tissues.** (Les lésions dégénératives des tissus tendineux et aponévrotiques)
J. DELARUE, J. MIGNOT, J. PAYEN, and A. ROUSSEL. *Presse médicale* [*Presse méd.*] **63**, 607–610, April 27, 1955. 9 figs., 12 refs.

In this paper from the Paris Faculty of Medicine attention is directed to changes in the state of the intercellular substance of tendinous and aponeurotic tissues in a variety of lesions, including synovial cysts (" ganglia "), tumours of tendon sheaths, lesions of knee-joint menisci, and Dupuytren's contracture. Of particular importance is the mucopolysaccharide material of the connective-tissue ground substance. The authors describe a histological study of tissue from 23 ganglia (mostly from the dorsum of the hand), 16 examples of tendon rupture, and 15 " histiocytic " tumours of tendon sheaths. Sections were stained with haemalum and eosin, Masson's trichrome stain, and toluidine blue or methylene blue to show metachromasia, as well as with the last two dyes at varying *p*H to assess the apparent isoelectric point of tissue constituents. The periodic-acid–Schiff technique was also used.

In all the conditions above referred to the abnormal connective tissue present showed a positive periodic-acid–Schiff reaction, metachromatic staining, and intensified staining with toluidine blue and methylene at a *p*H of about 3·5.

H. A. Sissons

1221. **Early Joint Lesions of Rheumatoid Arthritis. Report of Eight Cases, with Knee Biopsies of Lesions of Less than One Year's Duration**
J. P. KULKA, D. BOCKING, M. W. ROPES, and W. BAUER. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **59**, 129–150, Feb., 1955. 18 figs., 28 refs.

For a study of the early joint changes in rheumatoid arthritis biopsy specimens were taken from the synovial membrane of the knee from 7 days to 9 months after the onset of clinical involvement of the joint. The clinical and histological features of the 8 cases studied are described in detail. Pannus was present in only 3 cases. The lesions, which varied widely, are discussed under three headings: (1) generalized proliferative inflammation with intimal hyperplasia and inflammatory cell infiltration, chiefly lymphocytes with a focal distribution; (2) fibrin-like deposits and necrobiosis; and (3) vascular lesions, such as hyperplastic thickening of vessel walls and focal juxtavascular round-cell infiltration. Active vasculitis was found only in the biopsy specimen taken 7 days after the onset of joint involvement. The authors state that on the whole the lesions differed from those characteristically found in the fixed joints of the later stages of rheumatoid arthritis. In the earliest stages the reaction was confined almost entirely to the intima. Lymphocytic nodules and villous hypertrophy were seen in specimens taken more than 4 months after the onset. Some perivascular haemorrhage was also observed.

[The full account of this investigation repays detailed study.]

E. G. L. Bywaters

1222. **The Histological Aspects of Periarteritis Nodosa.** (Sur les aspects histologiques de la périartérite noueuse)
R. HABIB. *Annales de médecine* [*Ann. Méd.*] **56**, 352–436, 1955. 24 figs.

1223. **Lymphangiopericytoma. Case Report of a Previously Undescribed Tumor Type**
H. T. ENTERLINE and B. ROBERTS. *Cancer* [*Cancer* (*N.Y.*)] **8**, 582–587, May–June, 1955. 5 figs., 3 refs.

Microbiology and Parasitology

BACTERIA

1224. **Charcoal Agar Media for the Cultivation of *Mycobacterium tuberculosis***

J. W. WHALEN and W. L. MALLMANN. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 382–389, March, 1955. 11 refs.

Writing from Michigan State College, Lansing, Michigan, the authors describe a synthetic medium for the cultivation of tubercle bacilli of which the essential ingredient is activated charcoal; this acts by removing any long-chain fatty acids and lipids present which might inhibit growth. This medium was prepared with 4 different grades of charcoal and, together with similar media in which the charcoal was replaced by 0·2% bovine albumin, 10% human serum, or 10% Dubos oleic-acid–albumin complex, the generation time in hours of acid-fast bacilli grown on each medium was compared with that on the basic medium alone. These tests showed that the best medium was that enriched with bovine albumin, on which the generation time was reduced by 24·6%; media with one of the varieties of charcoal, human serum, and the oleic-acid–albumin complex were the next most effective, reducing the time by 20·8%. The charcoal has the advantage of being economical and also that it can be added to the medium before autoclaving.

The authors also experimented with the addition of ethyl violet to the medium in order to suppress contaminants. They found that in culturing pathological material a medium containing the most efficient of the four varieties of charcoal, penicillin, *cyclo*heximide, and 1 in 400,000 ethyl violet less frequently showed evidence of contamination than did orthodox Petragnani medium.

John M. Talbot

1225. **A Microcolonial Test for the Recognition of Virulent Mycobacteria**

I. KRASNOW, L. G. WAYNE, and D. SALKIN. *American Review of Tuberculosis and Pulmonary Disease* [*Amer. Rev. Tuberc.*] **71**, 361–370, March, 1955. 2 figs., 16 refs.

This report from the Veterans Administration Hospital, San Fernando, California, describes a test for the recognition of virulence in mycobacteria *in vitro* which makes use of the cording phenomenon described by Middlebrook *et al.* and the characteristic cytochemical reaction of virulent strains to neutral red solution described by Dubos and Middlebrook. Though these reactions have been stated to be positive in the case of all virulent mycobacteria, discrepancies have been reported by several workers, and the technique of the present authors was designed to permit observation of these two phenomena simultaneously and to evaluate them as a combined test for virulence of tubercle bacilli.

The organism is grown either on a " molecular filter " membrane or on a filter-paper strip placed on Löwenstein–Jensen medium in a moist atmosphere. When sufficient growth has occurred to be visible under the dissecting microscope the strip, or a portion of the membrane, is removed and stained with an acidified saturated alcoholic solution of neutral red for 10 minutes; sodium hydroxide or sodium carbonate is then applied as a " developer " and the stained microcolony is then mounted and examined microscopically. (The details of the technique vary slightly, depending on whether the specimen is supported on filter-paper or on membrane.)

All virulent strains of mycobacteria examined showed the cording phenomenon and also gave a positive reaction to the neutral-red test. Avirulent and saprophytic strains were negative in both tests or positive in one only, but never positive in both. Four strains of B.C.G. examined also gave a positive result in each case, although here the cording was of variable intensity. The authors conclude that a strain of *Mycobacterium tuberculosis* which gives a positive response to the neutral-red test and also displays the phenomenon of cording can be classified as virulent or potentially virulent.

John M. Talbot

1226. **The Detection of Tubercle Bacilli in Mouth Wash Specimens by the Use of Membrane Filter Cultures**

D. E. ROGERS, G. M. COOKE, and C. E. MEYERS. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 371–381, March, 1955. 3 figs., 7 refs.

The authors present a preliminary report from the University of California, Berkeley, California, on the development of a filtration technique for the recovery and culture of tubercle bacilli from patients who are unable to produce sputum. The method is as follows. The patient gargles and rinses his mouth and pharynx with 25 ml. of sterile buffered saline, which is then expectorated into a jar and treated to reduce the viscosity and eliminate buccal organisms by the application of 4% sodium hydroxide for 15 minutes, with subsequent neutralization. The treated fluid is then passed through a filter membrane of cellulose ester film under negative pressure at rates varying between 50 and 100 ml. per minute, after which the filter is removed and laid in a Petri dish on Löwenstein–Jensen medium or the oleic-acid–albumin–agar of Dubos and incubated at 37° C.

Under these conditions growth was found to proceed satisfactorily but at a slower rate than upon medium incubated directly, visible colonies appearing in 14 to 21 days on the filter and in 10 to 14 days on directly inoculated control plates. An insufficient number of specimens from patients with positive sputum but negative gastric aspirate cultures have so far been examined to permit of any statement regarding the sensitivity of the procedure under these circumstances. But the method has the advantage of much greater ease in collecting the specimen and in examining large quantities

of material such as urine or pleural fluid. Because of the delay in diagnosis due to the slow growth of tubercle bacilli the authors are now investigating a method of detecting microcolonies of the organism by direct staining on the membrane after only 4 to 6 days of incubation.

John M. Talbot

PROTOZOA

1227. **The Pre-erythrocytic Stage of *Plasmodium ovale***
P. C. C. GARNHAM, R. S. BRAY, W. COOPER, R. LAINSON, F. I. AWAD, and J. WILLIAMSON. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **49**, 158–167, March, 1955. 11 figs., 20 refs.

At the London School of Hygiene and Tropical Medicine the authors have investigated the character of pre-erythrocyte schizogony of *Plasmodium ovale* and give a full account of the tissue stages of the parasite. The strain of *P. ovale* used, which originated in Liberia, was first passaged through 2 hospital patients and then through a series of volunteers (including the authors themselves) until a heavy gametocyte infection appeared. A final volunteer was inoculated with sporozoites by bites from 750 infected mosquitoes (*Anopheles maculipennis*) on three occasions. Liver biopsy was carried out 9 days after the first exposure to mosquito bites.

The clinical course of the infection was severe; in all but 4 of the subjects the fever was tertian in its periodicity, with successive peaks over 105° F. (40·6° C.). The paroxysms were checked by chloroquine, but relapses followed in several of the sporozoite-induced infections. Examination of fresh blood infected with *P. ovale* did not reveal any oval cells, although these were observed in fixed and stained thin blood smears. From this it is concluded that the occurrence of oval cells is due to an artefact in the preparation of blood smears, but it is not suggested that this conclusion lessens the diagnostic value of the artefact. More than half the cells invaded by the parasite were reticulocytes. A striking feature was that this strain of *P. ovale* produced very large schizonts during relapses, each mature schizont containing 12 to 14 nuclei, that is, double the usual number.

Examination of some 4,000 serial sections of the liver biopsy specimen from the last patient revealed 8 complete pre-erythrocytic schizonts ranging from 28 to 60μ in length; they were provisionally termed "fifth-day schizonts". These immature schizonts were oval in shape, although as growth continued convolutions appeared. The nuclei were unusually large (2μ in diameter) and sometimes appeared to be composed of a number of granules. The schizont often resembled analogous coccidian forms, as the cytoplasm was collected around each nucleus and appeared to be vacuolated; the edge of the parasite was limited by a membrane. Owing to the distortion of the host cell caused by the large size of the schizont the exact type of cell invaded could not be identified, but was thought to be a parenchymal cell. The more mature schizonts, termed by the authors "ninth-day pre-erythrocytic schizonts", were larger (70 to 80$\mu \times 50\mu$) and markedly lobulated. The nuclei were smaller than those of the fifth-day forms and showed some symmetry in their arrangement. Merozoites did not appear simultaneously throughout the schizont, but developed first at its extremities. The merozoite was large (1·8μ in diameter) and spherical in shape, with a crescentic or rod-shaped nucleus situated to one side. The length of the pre-erythrocytic cycle was 9 days.

Summing up, the authors state that the pre-erythrocytic schizont of *P. ovale* resembles that of *P. falciparum* in its large size and bizarre contour, but the details of development, the nuclear structure, and the merozoites are quite different, as are also some of the staining reactions, and these provide a useful differentiating feature. The authors consider that the explanation of the extreme lobulation of the schizont of *P. ovale* lies in the amoeboid nature of this parasite.

R. A. Neal

SEROLOGY AND IMMUNOLOGY

1228. **A Serological Reaction in Malignancies**
W. F. EISENSTAEDT. *Journal of the National Cancer Institute* [*J. nat. Cancer Inst.*] **15**, 439–448, Dec., 1954.

On the assumption that a malignant tumour may produce an immunological reaction in the human body experiments were carried out at Manor Hospital, Chicago, to develop a serological test for malignancy, preparations from the heart, liver, kidney, and spleen obtained at necropsy on patients who died from cancer being used as "antigens". While the experiments with material from the heart, liver, and kidney were unsuccessful, suitably prepared extracts of spleen, when mixed with the serum of persons suffering from malignant disease, gave rise to flocculation reactions. Accordingly a procedure was developed which appeared to provide the basis for a simple serological test for the detection of cancer. [For details the original paper should be consulted.] The results of the test as applied in 6,500 cases are given in tables. They are held to justify the author's claim that the technique, which is still in the early stage of development, is a "satisfactory preliminary step in the establishment of a diagnostic test".

L. A. Elson

1229. **Tetanus Immunization XI. Study of the Duration of Primary Immunity and the Response to Late Stimulating Doses of Tetanus Toxoid**
J. C. PETERSON, A. CHRISTIE, and W. C. WILLIAMS. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 295–303, March, 1955. 11 refs.

The antibody response to various doses and types of tetanus toxoid and the blood antitoxin level in 219 volunteers at the Veterans Administration Hospital, Nashville, Tennessee, who had been actively immunized with tetanus toxoid a few months to 13 years previously, are reported.

A blood level of more than 0·1 unit per ml.—a level generally accepted as adequate to prevent the development of clinical tetanus—was found in all the subjects when the interval between the last antigenic stimulus

and estimation of the blood level was less than 3 years, in 68·4% when this interval was 4 to 8 years, in 59·4% when it was over 9 years, and in 83·9% of a miscellaneous group in which this interval was not known. The value of booster doses in the production of a high antitoxic immunity was obvious. A blood level of more than 0·1 unit per ml. was found in 43·4% of those who had received primary immunization only, in 75·8% of those who had received one booster dose, and in 84·8% of those who had received two booster doses.

The subjects were divided into 4 equal groups and the response to a fresh toxoid injection was studied, two of the groups receiving 0·25 ml. and 0·5 ml. respectively of fluid toxoid and two receiving similar doses of adsorbed toxoid. Blood samples for antitoxin titration were taken 6 or 7 and 13 or 14 days after the injection. Irrespective of the dose and type of toxoid given, a titre of 1 unit of antitoxin per ml. of blood was observed in 187 out of 208 subjects by the 6th or 7th day and in 205 out of 206 by the 13th or 14th day. In one subject whose blood antitoxin level by the 14th day was between 0·1 and 0·3 unit per ml. the initial antitoxin titre had been less than 0·01 unit per ml.; no booster dose had been given at any time and the stimulating injection in this case was 0·5 ml. of adsorbed toxoid.

A comparison of the response to each of the 4 stimuli revealed that dosage was not a significant factor, but when more than 9 years had elapsed since the last toxoid injection the response was more prompt with fluid than with adsorbed toxoid.

The authors recommend a booster injection within 5 years of primary immunization and after that tertiary booster doses about every 10 years. They conclude that subjects " not in shock are able to respond adequately to stimulating injections of tetanus toxoid at any time within 11 years after an approved tetanus immunization or the last antigenic stimulation " and that there is " no justification for giving prophylactic tetanus antitoxin ".

L. J. M. Laurent

1230. On the Existence of an Antibacterial Factor in Diphtheria Immunity. [In English]

H. LAUTROP. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **36**, 274–288, 1955. 4 figs., 21 refs.

To the small amount of indirect evidence supporting the hypothesis that an antibacterial factor plays a part in diphtheria immunity in addition to the antitoxic factor, direct experimental evidence is now added in this paper from the State Serum Institute, Copenhagen.

The general plan of the experiments was to immunize guinea-pigs actively with live cultures of non-toxigenic strains of *Corynebacterium diphtheriae* and to challenge the animals thus immunized with cultures of toxigenic strains, taking care in the first place that the toxigenic and non-toxigenic strains used possessed identical thermolabile surface antigens (K antigens). It was assumed that antibacterial immunity, if any developed, would check the local multiplication of diphtheria bacilli at the site of infection, and for greater ease of observation, and because the infection produced progressed slowly and therefore gave the antibacterial defence mechanism a longer period in which to act, the method of superficial skin infection described by Orskov (*Acta path. microbiol. scand.*, 1948, **25**, 829) was used for challenge. Immunization was carried out by giving, at weekly intervals, 4 subcutaneous and 3 intraperitoneal injections of 10,000 million organisms in a saline suspension made from a 20-hour culture of the non-toxigenic strain on ascitic agar, the challenging infection being given 6 to 14 days after the last immunizing injection.

In 3 experiments on 30, 30, and 20 immunized guinea-pigs and 20, 30, and 20 non-immunized controls respectively the survival rates on the 5th day were 34, 74, and 70% respectively amongst the immunized, whereas all the controls had died. After 14 days the survival rates among the immunized had fallen to 24, 50, and 50% respectively. After that time no further deaths occurred, but all survivors showed local necrosis of varying degree, which was proof of successful infection. The possibility that the protection was due to the production of antitoxin by the immunized guinea-pigs was excluded by a number of careful experiments. No protection was afforded by a polyvalent vaccine of *Escherichia coli* given in place of the diphtheria vaccine, showing that the protection provided by the latter could not be attributed to non-specific stimulation of the natural defence mechanisms. In 2 further experiments in which the strains of *C. diphtheriae* used for immunization and challenge had different thermolabile K antigens it was found, contrary to expectation, that the same degree of protection was provided. The author concludes that antibacterial immunity in diphtheria is probably not type-specific.

The demonstration of the existence of antibacterial immunity in diphtheria is of some theoretical interest since it must play some part in the complex parasite-host relationship which determines the outcome of an infection. It is emphasized, however, that it does not detract from the overwhelming clinical importance of antitoxic immunity from the point of view both of prophylaxis and treatment.

K. Zinnemann

1231. Comparison of a Hemagglutination Procedure and the Rabbit Intradermal Neutralization Test for the Assay of Diphtheria Antitoxin in Human Sera

M. LANDY, R. J. TRAPANI, R. FORMAL, and I. KLUGLER. *American Journal of Hygiene* [*Amer. J. Hyg.*] **61**, 143–154, March, 1955. 1 fig., 13 refs.

A study was made of the activity of 19 commercially prepared diphtherial antigens in modifying tannic acid-treated erythrocytes for agglutination by diphtheria antitoxin. It was shown that these products varied markedly in their effectiveness as antigens in the hemagglutination procedure. The presence, during the sensitizing process, of relatively inactive toxoids suppressed sensitization of erythrocytes by toxoids of high activity. The hemagglutination activity of certain toxoids was improved following electrodialysis.

One hundred and sixteen sera collected from human beings before or after immunization with diphtheria toxoid were assayed for antitoxin by the rabbit intradermal neutralization test (at 0·5 log intervals) and by a

standardized hemagglutination test (at 0·1 log intervals). The values obtained by these two procedures, plotted as the log of the reciprocal of the hemagglutination titer and the log of the units antitoxin, were indicative of a linear relationship. Analysis of variance showed that this relationship was significant at the 0·1% level. The results obtained indicate that the hemagglutination test may provide an acceptable alternate procedure for the assay of diphtheria antitoxin in human sera.—[Authors' summary.]

1232. **Immunization of Man against Epidemic Typhus by Infection with Avirulent *Rickettsia prowazeki* (Strain E). II. The Sero-immune State and Resistance to Virulent Challenge Two Years after Immunization and a Note as to the Nature of Immediate Postvaccination Reactions. III. The Serologic Response and Occurrence of Post-vaccination Reactions in Groups Vaccinated under Field Conditions in Peru**

J. P. Fox, M. E. Jordan, D. P. Conwell, T. A. Robinson, J. A. Montoya, and M. Espinosa M. *American Journal of Hygiene* [*Amer. J. Hyg.*] **61**, 174–182, 183–196, March, 1955. 10 refs.

In the first of these two papers the authors report further investigations carried out on a group of human volunteers who had been inoculated with an avirulent strain of *Rickettsia prowazeki* (Strain E) (*Amer. J. Hyg.*, 1954, **59**, 74). Of 125 prison inmates originally immunized, 44 were still available 2 years later. Five of these did not develop typhus when subjected to a challenge inoculation of a virulent strain (Breinl) of *R. prowazeki*, whereas 2 non-immune controls did. Three men immunized 9 months previously with a Cox-type vaccine were also challenged with the virulent strain, and in 2 of these the disease developed. On examination of sera from all 44 men by complement-fixation and neutralization tests it was found that there had been very little reduction in titre during the second year. When an attempt was made to identify the factor responsible for the immediate post-vaccination reactions which sometimes follow inoculation of Strain-E rickettsiae it was found that the factor was removed by centrifugation at 10,000 r.p.m. for one hour, suggesting that it is particulate and intimately related to the rickettsiae; but attempts to neutralize the factor with antisera were unsuccessful. It also seems unlikely that the factor is identical with those responsible for the toxicity of the vaccine in mice and the haemolysis that occurs *in vitro*.

The second paper is a supplement to the report on a large-scale field trial of the vaccine started in 1953 in Peru and covering about 16,000 persons (not yet published). An additional 1,682 individuals have been immunized, of whom 543 have been tested for serological response. It was found that quite small doses—4·0 to 4·5 log egg infective doses (E.I.D.)—produced a detectable serological response in more than 95% of those vaccinated, and that larger inocula produced a higher average level of antibody. An increased antibody titre was also noted in 90% of naturally immune individuals, but the increase was not related to the dose. In the authors' view, one of the principal problems arising from the use of the E strain of *R. prowazeki* is the fact that larger doses are more likely to produce immediate reactions. With a dose of 4·0 to 4·5 log E.I.D. it is estimated that there will be some 10 to 15% of immediate reactions and a similar proportion of delayed reactions; in only 1% of all persons inoculated has the reaction amounted to real illness. (This figure is higher, however, for older persons.) Some observations were also made on the nature of these reactions. Virtually no delayed reactions appear to occur in hitherto immune individuals, thus strengthening the earlier supposition that the delayed reaction is a true infection. The failure of previous immunization to prevent an immediate reaction suggests that it is not truly rickettsial in origin —a fact confirmed in the previous paper by attempts at neutralization *in vitro*. The stability of the lyophilized vaccine used appeared to be satisfactory, but as the period of observation has reached only 8 months, further study will be necessary.

A second phase of the trial is under way involving the vaccination of more than 10,000 persons, and the incidence of naturally occurring typhus in these will be compared with a similar number receiving a placebo injection.

R. F. Jennison

1233. **The Direct Flocculation of Influenza Virus**

G. Belyavin. *Lancet* [*Lancet*] **1**, 698–701, April 2, 1955. 5 figs., 14 refs.

A simple quantitative flocculation test for influenza virus is described in this paper from University College Hospital, London. Influenza-A virus (PR8, FM1, and Ashby strains) and influenza-B virus (Lee strain) were grown in developing eggs. The suspensions consisted of allantoic fluid clarified by centrifugation at 8,000 *g.* for 15 minutes, saline suspensions of virus deposited by high-speed centrifugation, and saline suspensions of virus which had undergone one cycle of adsorption and elution from chicken erythrocytes. Serum was prepared by intravenous injection into rabbits of 300 haemagglutinating units followed after 3 weeks by a second injection of ten times this dose; samples of serum were removed when found to be reactive.

For the flocculation test serial dilutions of serum were prepared in Dreyer tubes, equal volumes of virus suspension added, and the mixtures incubated at 37° C. When antibodies were present a faint opalescence appeared within a few minutes, followed by a fine granular precipitation and, later, well-marked flocculation which was clearly visible to the naked eye. Direct titration and cross-absorption tests showed that the reaction was specific. Comparative titrations with virus suspensions containing approximately the same number of agglutinating units but prepared in various ways showed that flocculation was minimal with crude allantoic fluid, more marked with suspensions of virus purified by high-speed centrifugation, and even more marked with virus suspensions purified by adsorption and elution from erythrocytes.

The author suggests ways in which the technique may be of value in the study of immunity to virus infections.

R. Hare

Pharmacology

1234. **A Purpuric Drug Eruption Caused by Carbromal**
P. BORRIE. *British Medical Journal* [*Brit. med. J.*] **1**, 645–646, March 12, 1955. 1 fig., 9 refs.

Carbromal is a hypnotic chemically related to chloral and bromvaletone. It is becoming increasingly popular as a sedative to be used at night, and in Britain can be purchased by the general public without a doctor's prescription. The drug was first introduced in 1910, but the first report that it caused an eruption of a purpuric nature appeared only in 1921. It is usually cited among drugs capable of causing purpura, but there is no general agreement about this.

The author describes 6 cases of drug eruption caused by carbromal observed at St. Bartholomew's Hospital, London. The eruption was remarkably constant in all 6 cases, and there were well-defined patches on the legs, buttocks, trunk, and upper arms consisting of petechiae and purpuric streaks, erythema, pigmentation, and branny scaling. Five of the patients complained of severe irritation. The dosage of carbromal varied, but in all cases was within the therapeutic range and bore no relation to the severity of the symptoms. Increased capillary fragility was uniformly observed, but there were no other haematological abnormalities. The author states that the condition may be mistaken for pityriasis rosea, seborrhoeic dermatitis, or eczema if the purpuric element is not recognized. He finds that the symptoms clear completely within a month at the most on stopping administration of the drug. *R. Wien*

1235. **Hypnotic Effects of an Antihistamine—Methapyrilene Hydrochloride**
B. STRAUS, J. EISENBERG, and J. GENNIS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 574–582, March, 1955. 9 refs.

Studies of the hypnotic effect of methapyrilene hydrochloride were made on 54 male patients who were under treatment at the Veterans Administration Hospital, Bronx, New York, for a wide variety of medical conditions and who were selected because of a persistent sleep disturbance. No patient was included who had physical symptoms severe enough to disturb sleep, who was a known reactor to placebos, who exhibited severe emotional disturbance, or who required narcotics. The patients were given, in random order, methapyrilene hydrochloride 50 mg., phenobarbitone 100 mg., and a placebo in capsules of identical appearance. For various reasons it was not possible to give each compound 6 times to each patient over a 3-week period as intended, but an average of 17 observations per patient was obtained. Response was assessed both subjectively and objectively, the latter by hourly observation with the aid of artificial light.

Methapyrilene and phenobarbitone exerted greater hypnotic effect than the placebo and were approximately equal in their effectiveness in inducing sleep; the patients could not distinguish between the two drugs, but objectively methapyrilene seemed the more potent. For maintenance of sleep, however, there was neither subjective nor objective difference between them. It is noteworthy that, although known placebo reactors were excluded from the trial, 30% of the patients attributed excellent sleep induction to the placebo.

The risk of granulocytopenia from methapyrilene, as from other members of the ethylenediamine group of antihistamines (for example, pyribenzamine), is probably low. One suicidal and one accidental death are quoted from the literature. No toxic effects were observed following the short and intermittent administration used in this trial. It is thought that, as with other antihistamines, tolerance to the sedative action of this drug might develop. *Bernard J. Freedman*

1236. **Effect of Largactil (Chlorpromazine) on Human Spasticity and Electromyogram. Preliminary Report**
J. V. BASMAJIAN and A. SZATMARI. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **73**, 224–231, Feb., 1955. 8 figs., 14 refs.

The effect of intravenous injections of chlorpromazine on the electromyogram of patients suffering from partial paralysis and spasticity due to an upper motor neurone lesion was investigated at the University of Toronto. All were long-standing cases. In 9 there was hemiplegia due to cerebral vascular accident or cerebral inflammatory disease, in one a high, bilateral, spinal-cord lesion, and in one a bilateral cervical-cord lesion. In one of the remaining 2 cases most of one cerebral hemisphere had been removed following trauma and in the other a temporal lobe had been removed because of brain abscess. A marked Parkinsonian tremor was an associated symptom in one case.

The standard procedure, where applicable, consisted in insertion of unipolar needle electrodes into the quadriceps femoris and observation of the electromyogram of the knee-jerk before and after the rapid intravenous injection of 50 mg. of chlorpromazine. Other muscles were used in cases unsuitable for this technique. During the tests the level of consciousness was noted and, in 6 cases, an electroencephalogram (EEG) was recorded.

In 11 of the 13 cases there was a dramatic reduction in spasticity within 3 minutes of the injection of chlorpromazine and the electromyograph became essentially normal; in the remaining 2 cases there was marked but incomplete improvement. The effect lasted for about 2 hours, and included reduction in or abolition of the phenomenon of "irradiation of stimuli". The EEG in 6 cases showed that the decrease in spasticity was not related to a decrease in consciousness, although most of the patients were drowsy. Chlorpromazine did not affect the residual or recovered voluntary activity of the muscles. The Parkinsonian tremor was abolished during the period of action of the drug.

The authors do not consider that the site of activity of chlorpromazine is at the myoneural junction, but rather that it is central, probably at mid-brain level. They suggest that parenteral administration of chlorpromazine may permit more rapid retraining of spastic limbs. *Kenneth Tyler*

1237. **Treatment of Intractable Pain with Large Doses of Morphine and Diamino-phenylthiazole**
F. H. SHAW and A. SHULMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 1367–1369, June 4, 1955. 8 refs.

The authors, writing from the University of Melbourne, describe a method of treating intractable pain by administration of large doses of morphine in conjunction with 2:4-diamino-5-phenylthiazole hydrobromide (D.A.P.T.), the latter drug relieving the respiratory depression and, in some cases, the vomiting and constipation produced by morphine without impairing its analgesic effect.

Increasingly large doses of morphine were given by intramuscular injection to 35 patients who had been receiving this drug every few hours, and 30 minutes after each injection 15 mg. of D.A.P.T. was administered intramuscularly, this procedure being continued until undue respiratory depression (or sedation) was evident or until analgesia lasting 6 to 8 hours was obtained. This process of "stabilization" took one or two days, the dosage of morphine to give 8 hours' analgesia being 32 to 162 mg. 2 to 4 times a day. Intramuscular injection of D.A.P.T. was then replaced by oral administration, 20 mg. (1 tablet) being given simultaneously with the injection of morphine. If the patient was too heavily sedated the oral dose of D.A.P.T. was increased to 30 or 40 mg. during the day, the dose at night being 20 mg. A barbiturate or an injection of hyoscine was also found to be desirable at night. During the stabilization period the patient was observed every 15 minutes for 2 hours following each injection of morphine. Dangerous respiratory depression—respiration rate below 6 to 8 a minute or shallow breathing accompanied by cyanosis—was relieved by intramuscular or intravenous injection of 10 mg. of D.A.P.T., repeated at 10-minute intervals, if necessary, until 60 mg. had been given. In this dosage D.A.P.T. caused no appreciable side-effects.

The authors found that it was easier to prevent the onset of pain than to alleviate it once it had begun, and the interval between injections was fixed accordingly. Administration of hyoscine and, to a lesser degree, of atropine during morphine–D.A.P.T. treatment increased drowsiness and, on occasions, prolonged analgesia; barbiturates, chlorpromazine, and the new anti-emetic "marzine" had no untoward effects. About one-quarter of the patients developed euphoria, although this was not observed during treatment with morphine alone. No signs of tolerance or addiction were noted in any of the 30 patients who received this treatment for periods up to 5 months. Moreover, there were no morphine-withdrawal symptoms, in marked contrast to the effect of administration of the other morphine antagonist, nalorphine.

The authors consider that D.A.P.T. is a specific antagonist of certain actions of the morphine group of drugs and of pethidine and methadone hydrochloride. It has no analgesic properties of its own, and appears to be a non-specific respiratory stimulant, especially when given parenterally, increasing the depth rather than the rate of respiration. The authors point out that because of the presence of a toxic impurity in some preparations of D.A.P.T. a toxicity test on rats should be carried out before the drug is employed clinically.

T. B. Begg

1238. **An Experimental and Clinical Study of a Synthetic Heparin-like Substance: Dextran Sulphate.** (Etude biologique et clinique d'un héparinique de synthèse: le sulfate de dextrane)
E. DONZELOT, H. KAUFMANN, and G. DAUZIER. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 1475–1480, April 30, 1955. 2 figs., bibliography.

The authors describe experimental and clinical studies carried out at the Pitié and Broussais Hospitals, Paris, with a new synthetic substance, dextran sulphate, of low molecular weight. In general the action of this substance resembles that of heparin, but differs in having more prolonged anticoagulant action, in showing an increasing duration of action on repeated injection, and in being fully effective by the intramuscular route. Electrophoretic studies showed that dextran sulphate has the same effect as heparin on serum lipids. It has the advantage of being much cheaper than heparin.

So far 60 patients have been treated with dextran sulphate; these have included a number with acute thrombotic episodes, who were treated intensively for a short period, and a group of patients with diseases of the coronary, cerebral, and peripheral arteries and others with recurring emboli, all of whom were treated for longer periods. For intensive treatment the authors gave, on the first day of the course, 3 intravenous injections each of 2·5 ml. of a solution of which 1 ml. was approximately equal in activity to 1,000 units of heparin. On the second day 2 similar injections were given, and thereafter one injection daily or every second day sufficed. In long-term treatment 2 injections per week, each of 2 ml., was found to be sufficient. Treatment was controlled by measuring the prothrombin time by both the Howell and the Quick methods every second day at first, then less frequently. Administration by intramuscular injection is also effective and painless, but is not advised as a routine because of the danger of causing the formation of haematomata.

Dextran sulphate proved very satisfactory, particularly in cases of ischaemic disease of the limbs, in which pain was promptly relieved and the temperature of the limb rose. The authors consider that such cases are the most suitable for treatment with dextran sulphate. Only one serious haemorrhagic incident occurred, which was treated by transfusion. The warning is given that protamine sulphate is not dependable as an antagonist of dextran sulphate. Side-effects of dextran therapy were few, but 6 of the patients receiving long-term treatment developed temporary alopecia; however, the hair began to grow again when treatment was stopped.

Bernard Isaacs

Chemotherapy

1239. **Changing Patterns of Resistance of Certain Common Pathogenic Bacteria to Antimicrobial Agents**
M. FINLAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 570–580, April 7, 1955. 9 figs., 18 refs.

From 1949 to 1954 inclusive a systematic study was undertaken at the Thorndike Memorial Laboratory, Boston, of the sensitivity to chemotherapy of a number of strains of pathogenic bacteria, and in the present paper the variations in drug resistance observed during this period are reported.

There was no important change in resistance to the antibiotics then available of Group-A haemolytic streptococci, *Haemophilus influenzae*, or strains of meningococcus, gonococcus, and *Proteus*. Strains of gonococcus isolated in 1954 were considerably more sensitive to sulphadiazine than those isolated in 1949, and this is attributed to the fact that penicillin had replaced sulphonamides in the treatment of gonococcal infections.

Strains of *Staphylococcus aureus* collected and tested at various times over a period of 10 years showed not only a progressive increase in the proportion which were resistant to penicillin, but also an increase in the degree of resistance to the antibiotic. About a quarter of the most recently isolated strains were resistant to chlortetracycline (aureomycin); even in the first series of strains tested more than a quarter were highly resistant to oxytetracycline, which was assumed to be the result of cross-resistance against aureomycin. None of the staphylococcal strains exhibited either a moderate or a high degree of resistance to chloramphenicol. Strains of *Pseudomonas* showed a definite increase in resistance to streptomycin and to neomycin and a slight increase in resistance to the broad-spectrum antibiotics.

The author states that most of the changes appeared to be directly correlated with the extensive use of the particular agent concerned, but some could only be explained on the basis of cross-resistance from other antibiotics. *E. G. Rees*

1240. **The Palliation and Remission of Cancer with Combined Corticosteroid and Nitrogen Mustard Therapy. A Report of 100 Cases**
W. D. MCCARTHY. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 467–476, March 24, 1955. 1 fig., 5 refs.

The results are described of the treatment of 100 cases of cancer, which had failed to respond to other forms of treatment, with large doses of ACTH or cortisone administered simultaneously with nitrogen mustard ("mustargen"; methyl bis-(β-chloroethyl)-amine hydrochloride). In 16 of the cases a remission lasting up to 3 years was obtained, often with regression or arrest of tumour growth; in another 15 cases palliation was achieved and life prolonged. It is claimed that the ACTH and cortisone acted by abolishing or reducing the nausea, vomiting, and bone-marrow depression which usually follow the administration of nitrogen mustard. Complications and side-effects of the treatment are stated to have been few and temporary. Clinical reports of 17 cases are given. *G. Calcutt*

1241. **Control of Neoplastic Effusion by Phosphoramide Chemotherapy**
J. C. BATEMAN, B. MOULTON, and N. J. LARSEN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 713–719, May, 1955. 4 figs., 6 refs.

An account is given of the treatment of 21 cases of serous-cavity effusion secondary to metastatic carcinoma by the intracavitary instillation of N:N′:N″-triethylene thiophosphoramide, and of 2 cases of mammary cancer given N-(3-oxapentamethylene)N′:N″-diethylene phosphoramide. Control of pleural effusion lasting one to 9 months was obtained in 10 out of 17 cases of mammary and ovarian cancer; pericardial and ascitic effusion was controlled in one case of ovarian cancer, and decrease in ascites obtained in 4 others. The use of phosphoramides as anti-tumour agents is discussed. *G. Calcutt*

ANTIBIOTICS

1242. ***In vitro* Studies on the Combination of Penicillin and Streptomycin.** [In English]
O. KYLIN and E. WALL. *Acta medica Scandinavica* [*Acta med. scand.*] **151**, 281–288, April 16, 1955. 2 figs., 11 refs.

Sensitivity tests were carried out at Södersjukhuset, Stockholm, using the method of Ericsson and Löfström (see *Scand. J. clin. Lab. Invest.*, 1954, **6**, Suppl., 11), to find out whether the synergistic activity of a penicillin–streptomycin combination is limited to specific bacterial strains, and to compare this activity with that of aureomycin, chloramphenicol, and oxytetracycline. The investigation embraced 245 different bacterial strains from cases of urinary-tract infection, 489 from cases of respiratory-tract infection, and 276 from cases of otitis. The paper disks used in the tests had a diameter of 5 mm. and contained, respectively, 20 i.u. of sodium benzylpenicillin, 50 μg. of streptomycin, 50 μg. of aureomycin, 30 μg. of chloramphenicol, 50 μg. of oxytetracycline, and a mixture of 30 i.u. of sodium benzylpenicillin and 50 μg. of dihydrostreptomycin sulphate.

The penicillin–streptomycin mixture showed a statistically significant synergistic action against less than half the strains tested, but never showed an antagonistic action. Except against *Escherichia coli* and enterococci, it was in general more effective than aureomycin, chloramphenicol, and oxytetracycline. The combination is recommended for the treatment of infections of

unknown aetiology, and to enable streptomycin dosage to be decreased in cases of streptomycin-sensitive infection that are resistant to penicillin. *J. E. Page*

1243. **Treatment of Whitlow with Intravenous Injections of Procaine Penicillin.** (К вопросу о комплексном методе лечения больных панарициями внутривенной новокаин-пенициллинотерапией)
V. J. Shlapobersky and K. H. Gubar. *Советская Медицина* [*Sovetsk. Med.*] 20–22, No. 4, April, 1955.

The authors describe the successful treatment of 168 out-patients suffering from non-specific infections of the fingers and wrist by the intravenous injection of procaine hydrochloride and penicillin. A tourniquet was applied to the lower part of the arm in such a way as to compress both arteries and veins, the skin was thoroughly cleansed with alcohol, and into a prominent vein on the dorsum of the hand 20 to 40 ml. of a 0·5% solution of procaine in which 100,000 to 200,000 units of penicillin had been dissolved was slowly injected, the point of the needle being directed towards the periphery of the hand. The tourniquet was kept on for another 7 to 10 minutes, by which time complete anaesthesia of the forearm, wrist, and hand had usually developed. Incisions and cleaning up of the infected area where necessary were carried out without further analgesia. The pain from the inflammation disappeared following the injection and generally did not recur. In some neglected cases repeated injections were required, but these too were well tolerated. After a suitable rest the patient was allowed to go home.

Laboratory investigation showed that the concentration of penicillin in the blood of the area reached by the injection ranged from 100 to 200 units per ml., a figure which compared favourably with a concentration of only 0·1 to 0·9 unit per ml. 15 to 20 minutes after the usual parenteral injection of penicillin. *A. Orley*

1244. **Variations in the Antimicrobial Activity of the Tetracyclines**
R. J. Reedy, W. A. Randall, and H. Welch. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **5**, 115–123, March, 1955. 6 refs.

This is a continuation of an earlier investigation carried out at the U.S. Department of Health, Washington, D.C. (*Antibiot. and Chemother.*, 1954, **4**, 741; *Abstracts of World Medicine*, 1955, **17**, 95) into the activity *in vitro* of chlortetracycline (aureomycin), oxytetracycline, and tetracycline against a number of Gram-negative and Gram-positive organisms.

Considerable differences in sensitivity to the three antibiotics were encountered in strains of *Staphylococcus*, *Aerobacter*, *Klebsiella*, *Escherichia*, *Salmonella*, *Shigella*, *Proteus*, and *Pseudomonas*. Generally, chlortetracycline was the most effective against Gram-positive cocci and tetracycline the most effective against Gram-negative bacilli. At some concentrations, however, oxytetracycline was more active than the other two against certain strains of organisms in both groups.

The results indicate that these three antibiotics do not possess "equal antibacterial activity" and that laboratory sensitivity tests are necessary to determine which will be the most effective in any particular infection. The authors state that all three are equally effective clinically against highly-sensitive organisms—including *Haemophilus influenzae*, β-haemolytic streptococci, pneumococci, gonococci, and perhaps meningococci—and in diseases due to certain large viruses and to rickettsiae. In the treatment of meningococcal meningitis tetracycline is of special value because it enters the cerebrospinal fluid more readily than chlortetracycline or oxytetracycline. *Derek R. Wood*

1245. **A Microbiological Comparison of Erythromycin and Erythromycin B**
W. E. Grundy, E. F. Alford, C. J. Rickher, R. R. Bower, E. J. Rdzok, and J. C. Sylvester. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **5**, 212–217, April, 1955. 1 fig., 4 refs.

A microbiologic comparison of erythromycin and erythromycin B demonstrated no significant difference in their antimicrobial spectra, in the effects of blood and serum, in their bactericidal properties, and in the treatment of *Str. pyogenes* and *D. pneumoniae* infections of mice. A study of resistance development covering five strains of *M. pyogenes* var. *aureus* indicated that resistance to erythromycin B was gained more readily than resistance to erythromycin.—[Authors' summary.]

1246. **Coliformin: Production and Isolation**
S. K. L. Freyschuss, S. O. Pehrson, and B. Steenberg. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **5**, 218–223, April, 1955. 8 refs.

Futher studies of a new, highly fungicidal antibiotic, coliformin, are reported. A liquid medium containing glucose, ammonium tartrate, phosphate, magnesium, and trace elements gives rapid growth and high yields of coliformin. The active principle, a polypeptide containing eight amino acids, has been isolated and characterized. Coliformin is active against a wide variety of fungi including plant and human pathogens.—[Authors' summary.]

1247. **The Emergence of Antibiotic-resistant Gram-negative Bacilli**
J. P. Sandford, C. B. Favour, and F. H. Mao. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 540–545, April, 1955. 11 refs.

At the Peter Bent Brigham Hospital, Boston, the sensitivity to antibiotics of strains of recently isolated Gram-negative bacilli causing genito-urinary infections was compared with that of similar strains isolated before 1946 and maintained in a lyophilized state in the American Type Culture Collection. It was shown that lyophilization in no way affected the antibiotic sensitivity of the organisms, which included *Aerobacter aerogenes*, various species of *Proteus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and miscellaneous coliform bacilli. They were cultured for 18 hours in broth containing concentrations of streptomycin, chloramphenicol, chlortetracycline (aureomycin), or oxytetracycline ranging from 2 μg. to 32 μg. per ml. The lowest concentration causing macro-

scopic inhibition of growth was regarded as the " sensitivity level ", and strains not inhibited by 32 μg. per ml. were considered to be resistant. All species showed an increased resistance to streptomycin, and *Aerobacter aerogenes* and strains of *Proteus* exhibited a significantly increased resistance to chlortetracycline and oxytetracycline. However, there did not appear to be any change in the number of strains which were sensitive to chloramphenicol. *E. G. Rees*

1248. **The Treatment of Mycoses Due to *Candida albicans* with a New Antibiotic Active against Fungi: " Nystatin ".** (Traitement des infections mycosiques à *Candida albicans* par un nouvel antibiotique antifongique: la nystatine)
E. DROUHET. *Presse médicale* [*Presse méd.*] **63**, 620–623, April 27, 1955. 6 figs., 22 refs.

The frequency and gravity of the pathological manifestations due to yeast-like fungi of the genus *Candida*, and especially those due to *Candida albicans*, have considerably increased during the last few years, and it has been suggested that this has coincided with the increased use of antibiotics in high dosage, as these seem to favour the multiplication of *Candida* on mucous membranes. Recently a number of workers have reported good results in the treatment of these conditions from the use of the new antibiotic " nystatin ".

After recalling the origin of this antibiotic and reviewing its main properties the author reports that in studies carried out at the Pasteur Institute, Paris, he has confirmed the activity of nystatin *in vitro* and *in vivo* and its complete absence of toxicity in therapeutic doses. Nystatin is active against all species of *Candida*, inhibiting their growth in concentrations ranging from 1·56 to 12·5 μg. per ml. The addition to the culture medium of antibiotics such as oxytetracycline, chloramphenicol, aureomycin, streptomycin, and penicillin had no effect whatsoever on the growth of species of *Candida* or *Geotrichum*. Nystatin was also shown to be fungicidal, a solution of 1,000 μg. per ml. killing all of 3×10^9 living *Candida albicans* per ml.

In experiments on rabbits, which are highly susceptible to *Candida albicans* infection, intragastric doses of nystatin ranging from 1·2 to 6 g. daily, or the intravenous administration of 25 mg. per kg. body weight produced no toxic signs. In rabbits infected with *Candida albicans* the administration intravenously or subcutaneously of 40 mg. of nystatin reduced the mortality, previously 100%, to 62%. Further, when 50 mg. of nystatin was given by stomach tube to infected rabbits examination of the faeces after 3 days showed that only a few yeast cells were present.

Clinically, very young children with *Candida* infections were treated with nystatin mixed with their food in doses of 0·1 to 0·2 g. per kg. body weight on the first day and 0·1 per kg. for the next 3 or 4 days with good results. In 35 cases of generalized or localized infections due to *Candida albicans* in children and adults nystatin proved to be remarkably efficacious. Digestive, urinary, and toxic troubles disappeared, buccal lesions subsided, and laboratory examination showed that *Candida* disappeared in 4 or 5 days. In only 3 out of the 35 cases did relapse occur 2 weeks after the treatment was stopped. The topical application of an ointment containing nystatin was also effective in the treatment of localized lesions. Nystatin was completely free from toxic effects.
E. Forrai

CHEMOTHERAPY OF TUBERCULOSIS

1249. **The Influence of Isoniazid and Streptomycin on Acid-fastness, Tetrazolium Reduction, Growth, and Survival of Tubercle Bacilli**
D. KOCH-WESER, W. R. BARCLAY, and R. H. EBERT. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 556–565, April, 1955. 5 figs., 13 refs.

The object of this investigation in the Department of Medicine, University of Chicago, was: (1) to determine whether loss of acid-fastness in tubercle bacilli due to isoniazid depends on the medium, and specifically on the presence of " tween 80 "; and (2) to study the influence of streptomycin and isoniazid on growth and metabolic activity of strains of tubercle bacilli both susceptible and resistant to the drug.

Tubercle bacilli of the H37Rv strain were inoculated in 4 different media: (1) Dubos tween–albumin for submerged growth; (2) the same medium without tween; (3) Proskauer and Beck medium for surface growth; and (4) Proskauer and Beck medium with the addition of tween. After growth, samples were taken and stained by the Ziehl–Neelsen method. Isoniazid was then added, and 10 days later more samples were removed and stained. To produce isoniazid-resistant bacilli the H37Rv strain was passed through medium containing increasing amounts of isoniazid. Multiplication of bacilli was followed by nephelometric readings, and to measure one aspect of the metabolic activity of the bacilli the reduction of triphenyl tetrazolium was followed by colorimetric readings of the formazan (reduced tetrazolium) produced. (The usefulness of the triphenyltetrazolium chloride reduction test for determining the metabolic activity of *Mycobacterium tuberculosis* has previously been demonstrated (*J. clin. Invest.*, 1952, **31**, 644).) It was found that the loss of acid-fastness of tubercle bacilli exposed to isoniazid *in vitro* was independent of the type of medium and of the presence of tween 80. The appearance of non-acid-fast rods in liquid tween–albumin medium was gradual and paralleled the slowing of growth rate and the decrease in tetrazolium reduction. Complete loss of acid-fastness was associated with failure of the cells to multiply when transferred to a favourable environment. Streptomycin-treated tubercle bacilli (10 μg. per ml.) showed complete inhibition of growth and of tetrazolium reduction almost immediately, yet their acid-fastness was not altered. Removed from streptomycin, the bacilli eventually resumed growth and the ability to reduce tetrazolium. It was concluded that under these experimental conditions *in vitro* streptomycin was bacteriostatic, whereas isoniazid was bactericidal. *R. Wien*

Infectious Diseases

VIRUS INFECTIONS

1250. **Factors Predisposing to Poliomyelitis. The Possible Role of Other Infectious Diseases of Childhood and Particularly of Whooping-cough.** (A propos des facteurs favorisants de la poliomyélite. Le rôle éventuel des autres maladies infectieuses infantiles et tout spécialement de la coqueluche)
A. GROSSIORD, J. P. HELD, and J. LEBOURGE. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **71**, 306–312, March 11, 1955. 3 figs., 9 refs.

The case histories of 264 children under 10 years of age recovering from poliomyelitis at the Rehabilitation Centre, Garches (Versailles), were examined for evidence of infectious diseases contracted in the 3 months preceding the onset of the poliomyelitis. Among other infectious diseases, such as mumps and chicken-pox, the authors noted that whereas there were only 4 cases of measles, there were 18 of pertussis. The ratio between these (1 to 4·5) is the reverse of that reported by the French National Institute of Hygiene, which for 1953 received notification of 14,427 cases of measles and 4,671 of whooping-cough, a ratio of 3 to 1. Although they admit that 9 of the 18 cases of pertussis had received intramuscular injections during treatment, they nevertheless conclude that whooping-cough is a factor predisposing to poliomyelitis. *J. E. M. Whitehead*

1251. **The Vital Capacity as a Measure of the Spontaneous Breathing Ability in Poliomyelitis**
B. G. FERRIS, A. WARREN, and C. A. BEALS. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 618–621, April 14, 1955. 1 fig., 5 refs.

The investigation described in this paper from Harvard School of Public Health, Boston, was undertaken to obtain further information concerning the optimum time at which patients suffering from respiratory-muscle paralysis should be placed in a respirator. Vital capacity was determined in 3 patients with acute poliomyelitis and 56 who were convalescent from the disease, measurements being taken with the patient supine and volumes corrected for body temperature, ambient pressure, and water-vapour content. Vital capacity in adults was compared with the predicted value as determined from the regression equations of Baldwin, and that in children from Ferris's data. A fall of 15 to 20% in the vital capacity during unassisted breathing was taken to represent "fatigue". In some patients with a low vital capacity signs of distress developed in the absence of a further fall. A rise of 15 to 20% in the pulse rate, respiratory rate, or blood pressure was an early sign of ventilatory insufficiency and the test was stopped. The "unassisted breathing time" was determined by the patient's subjective response and the clinical signs. A graph is reproduced in which the initial vital capacity as a percentage of the predicted value is plotted against the unassisted breathing time without fatigue. A vital capacity of 10% of that predicted did not allow unassisted breathing, but unassisted breathing time rose greatly with small increases in vital capacity. The minimum vital capacity which permitted unassisted breathing for as long as 24 hours was generally 30 to 35% of the predicted value, with wide individual variations.

The value of early temporary use of the tank respirator in cases of acute poliomyelitis is emphasized. It is pointed out that the patient then becomes familiar with the apparatus without the extreme fear and apprehension associated with the loss of respiratory function, and the problem of re-establishing unassisted breathing is made easier. During the acute stage fever and anxiety must be considered when estimating the need for assisted breathing. *E. H. Johnson*

1252. **An Evaluation of the 1954 Poliomyelitis Vaccine Trials. Summary Report**
T. FRANCIS, R. F. KORNS, R. B. VOIGHT, M. BOISEN, F. M. HEMPHILL, J. A. NAPIER, and E. TOLCHINSKY. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **45**, 1–63, Part II, May, 1955. 12 figs.

1253. **The Involvement of the Heart in Poliomyelitis.** (Herzbeteiligung bei Poliomyelitis)
G. SCHAPER and B. S. SCHULTZE-JENA. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **76**, 91–106, 1955. 5 figs., bibliography.

Involvement of the heart in poliomyelitis, as judged by excessive tachycardia or bradycardia, has been known for over 40 years, but has been reported more frequently since it became possible to study the electrocardiogram (ECG) in such cases. An analysis of various authors' reported figures revealed that of a total of 1,600 cases investigated, 27% showed ECG abnormalities (range 10·5 to 55%), and in 420 cases of poliomyelitis in children the average incidence was 33·1% (range 4·2 to 52%).

The present authors, working at the Children's Clinic of the University of Münster, Westphalia, undertook electrocardiographic investigations in 54 out of 150 children admitted to hospital with poliomyelitis during an epidemic in the summer of 1952. In the majority of cases the ECG was recorded soon after the diagnosis was established; follow-up studies were not possible. In 28 of these cases (51·8%) pathological tracings were obtained which showed a wide variety of changes, including sinus bradycardia and tachycardia, changes in the QRS complex, prolongation of the Q–T interval, flattening of the T waves, ventricular and auricular extrasystoles, and abnormalities of the S–T segment. There was no difference in the incidence of these changes in

the various forms—spinal, bulbar, and non-paralytic—of the disease. Extrasystoles and nodal rhythms were recognized clinically.

In 4 fatal cases histological examination of the heart showed that polymorphonuclear leucocytes were present in the perivascular tissues in 2 cases and were diffusely distributed in the interstitial tissue in the 3rd, these findings being indicative of early myocarditis; in the 4th case no microscopic lesion was found. Macroscopically, enlargement and dilatation of the heart, subpericardial petechiae, and pallor of the myocardium were noted.

The aetiology of the ECG changes could not be determined, but many possibilities are considered on the basis of the authors' own experience and on the evidence reported by other workers. It is considered that the most important possible causes include a direct effect of the poliomyelitis virus on the cardiac muscle, secondary changes due to pulmonary involvement, metabolic disorders, and disturbance of the regulatory mechanism through involvement of the central nervous system.

[It must be a matter of opinion whether certain of the ECG changes here described should be regarded as anything other than non-specific manifestations of a feverish illness, or even as variants of the normal.]

John Lorber

1254. **Vaccination against Paralytic Poliomyelitis: Performance and Prospects**

J. E. SALK. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **45**, 575–596, May, 1955. 21 figs.

1255. **Nonbacterial Regional Lymphadenitis ("Cat-scratch Fever"). An Evaluation of the Diagnostic Intradermal Test**

J. J. MCGOVERN, L. J. KUNZ, and F. M. BLODGETT. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 166–172, Feb. 3, 1955. 4 refs.

In an attempt to evaluate the use of skin-test antigens in the diagnosis of non-bacterial lymphadenitis ("cat-scratch fever") the authors carried out tests in 18 clinical cases of the disease and in several groups of control subjects at the Massachusetts General Hospital, Boston. Three antigens were prepared from pus aspirated from lymph nodes in 3 cases and a 0·1-ml. dose was injected into the skin of the forearm of each subject tested. Within 10 minutes a weal appeared which lasted 24 hours in most cases, but this non-specific response had disappeared at 48 hours. The reaction was considered to be positive if there was an indurated papule 4 mm. in diameter and a zone of erythema 1 cm. or more in diameter.

It was found that all the 18 patients gave a positive reaction to one or more antigens. A positive result was also obtained in 4 (10·5%) of 38 members of the families of these patients, in one out of 21 members of healthy families, in 4 (22·2%) of 18 persons working in an animal hospital, and in one out of 22 members of the hospital staff. The higher ratio of positive reactions in the personnel of the animal hospital, although suggestive, might easily be due to chance in the numbers tested.

The authors conclude that the demonstration of positive reactions with skin-testing materials, as at present prepared, is of little value in the diagnosis of non-bacterial lymphadenitis in the absence of well-defined clinical signs and symptoms.

Thomas Anderson

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1256. **ACTH-treatment in Acute Hepatitis.** [In English] K. KIRKEBY, H. PALMER, O. RÖMCKE, and J. H. SOLEM. *Gastroenterologia* [*Gastroenterologia* (*Basel*)] **83**, 148–156, 1955. 2 figs., 17 refs.

At Drammen Hospital, Norway, ACTH was tried in the treatment of 38 patients suffering from acute hepatitis. The drug was administered by intravenous infusion in a daily dosage of 12·5 to 25 i.u. or by intramuscular injection of 100 i.u. a day initially and smaller doses subsequently. Usually treatment was begun 20 days after symptoms developed and was continued until the icterus index and serum prothrombin value were normal. In all the patients there was a fall in the icterus index with a rise in the prothrombin level within a few days of the start of treatment. Complications throughout were negligible.

[This series was uncontrolled, so few deductions can be made. The indications for corticotrophin therapy in acute virus hepatitis are slender, and the position is not clarified by this paper.] *D. Geraint James*

BACTERIAL INFECTIONS

1257. **Treatment of Typhoid with Synnematin B. Preliminary Report**

L. BENAVIDES, B. H. OLSON, G. VARELA, and S. H. HOLT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 989–994, March 19, 1955. 9 refs.

In this preliminary report from the Hospital Infantil, Mexico City, is described the treatment of typhoid fever in 16 children with a new antibiotic, synnematin B. This drug has a definite specific effect *in vitro*, and the clinical response to it appears to be as satisfactory as that to chloramphenicol. In so far as the limited data go, however, synnematin B in suitable dosage appears to have a bactericidal rather than a bacteriostatic effect, and may possibly be superior to chloramphenicol as regards relapses and the carrier state. But before this suggestion can be accepted a much larger trial is necessary. The authors undertake to carry out such a trial, giving particular attention to dosage, period of treatment, and methods of administration other than intramuscular injection as used in the present series.

Synnematin B was isolated from *Tilachlidium* in 1951 (*Proc. Soc. exp. Biol.* (*N.Y.*), 1951, **76**, 307). It is highly active against a variety of *Salmonella* strains *in vitro*, and against *S. typhosa* and *S. typhimurium* in mice and *S. pullorum* in chicks. In one experiment it proved to be the most effective of 5 antibiotics tested *in vitro* against 40 strains of *S. typhosa*. It does not appear to be toxic for human beings.

The 16 patients in this series (15 with typhoid and one with paratyphoid A) were severely ill and suffering from malnutrition. Three dosage schedules were used —20 mg., 40 mg., and 87·5 mg. per kg. of body weight. The first two were exploratory and gave blood levels less than, or about equal to, the sensitivity levels (1 unit per ml.) as determined *in vitro*. The third group contained only 3 patients, and in this group the blood levels ranged from 1 unit to 8 units per ml. Three of the cases were relapses and there was one persistent case—in a very poorly nourished and severely ill child. There were no instances of intestinal haemorrhage or perforation and no deaths, and the carrier state was not observed in any patient up to 3 months after treatment. No toxic effects of the drug were observed except for a chill reaction which seemed to be associated with a large loading dose, although the possibility that the preparation contained impurities could not be ruled out.

[The report on further investigations will be awaited with interest.] *H. Stanley Banks*

1258. **Erythromycin in the Treatment of Whooping-cough.** (L'eritromicina nella terapia della pertosse)
G. R. Mitolo. *Aggiornamento pediatrico* [*Aggiorn. pediat.*] **6**, 123–132, March, 1955. 1 fig., 19 refs.

The author states that erythromycin shows *in vitro* a high degree of activity against *Haemophilus pertussis*, and in view of its low toxicity in comparison with other antibiotics he has therefore used it at the University Paediatric Clinic, Genoa, in the treatment of 18 children with whooping-cough. The antibiotic was administered either by mouth or by the inhalation of a nebulized solution. The patients, whose ages ranged from 4 months to 9 years, received a daily oral dose of 30 to 40 mg. per kg. body weight (8 to 10 mg. 6-hourly) for 10 to 12 days. For aerosol therapy the dose was 200 mg. of the drug, 100 mg. being given twice daily. No side-effects were produced by either type of therapy and both methods of treatment showed the same good results, the children usually recovering in from 10 to 20 days. The author is confident that aerosol therapy with erythromycin could be extended with good results to the treatment of other diseases of the upper respiratory tract produced by organisms sensitive to this drug.

Franz Heimann

SARCOIDOSIS

1259. **The Treatment of Boeck's Sarcoidosis of the Lungs with Cortisone.** (Zur Cortisonbehandlung der Boeckschen Sarcoidosis der Lungen)
E. Sommer. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **85**, 215–222, March 5, 1955. 6 figs., bibliography.

At the Braunwald Sanatorium, Switzerland, during 1953 the author treated 3 female patients aged 32, 37, and 42 suffering from advanced sarcoidosis of the lungs with total doses of cortisone ranging from 4·7 to 8·7 g. Before treatment the patients had been coughing incessantly, losing weight, were intensely dyspnoeic with a diminished vital capacity, and had become pale, pyrexial, and exhausted. The radiological appearances showed coarse pulmonary mottling, pseudo-cavitation, and obstructive emphysema. Within 7 days of the start of treatment with cortisone there was a dramatic improvement in their general condition, with cessation of the non-productive cough, amelioration of the dyspnoea, a slight increase in vital capacity, and some gain in weight; there was, however, no improvement in the radiological picture. When cortisone was stopped all 3 became depressed, and some months afterwards the condition in one case was considered to have returned to its original state and in the other 2 to have deteriorated greatly, both these patients having developed right heart failure.

Taking these 3 cases as a point of departure the author reviews the literature and suggests that a more exact classification of sarcoidosis into (I) a pre-granulomatous stage, (II) a granulomatous stage, and (III) a hyalinizing and fibrotic stage would allow of better assessment of the indications for cortisone administration. He states that histiocytes and lymphocytes abound in early lesions, and that in Stages I and II spontaneous cure with regression of the lesion is frequent. In sarcoidosis of the skin, muscles, and lymph nodes satisfactory "healing" may even occur in Stage III. In pulmonary sarcoidosis, however, hyalinization in Stage III leads irrevocably to disabling fibrosis; in this manifestation of the disease, therefore, cortisone is indicated only before fibrosis has begun, when it may further the natural tendency of the condition to regress, and help to prevent hyalinization and fibrosis. If administered in Stage III cortisone actually promotes fibrosis and may thus hasten the supervention of pulmonary tuberculosis.

Discussing problems of diagnosis the author suggests that for a definite diagnosis of sarcoidosis of the lung parenchyma to be made histological examination of the middle lobe of the right lung may be necessary; this also reveals the stage to which the disease has progressed. The hilar lymph nodes may be diseased without involvement of the lung parenchyma, but in any case lesions in both tissues tend to heal spontaneously and to react poorly to cortisone. Radiography is not very helpful in assessing the stage of the condition; reticulated and miliary mottling probably indicate Stage II, and coarse mottling with focal shadows Stage III. Measurement of the vital capacity is also only a rough clinical guide to the degree of pulmonary fibrosis present. As many fresh cases of pulmonary sarcoidosis heal spontaneously without cortisone, they should be observed for a time under sanatorium conditions. The dosage of cortisone should be kept as low as possible, beginning with 100 to 150 mg. daily according to individual requirements, later falling to a daily maintenance dose of 50 to 75 mg., and being gradually reduced before finally stopping treatment. Cortisone is contraindicated in patients with diabetes, hypertension, cardiac disease, and osteoporosis. Withdrawal of the hormone may lead to psychosis, increased liability to infection, and even respiratory failure, and these disadvantages must be weighed carefully against its advantages when its administration for the treatment of pulmonary sarcoidosis is being considered. *E. S. Wyder*

Tuberculosis

DIAGNOSIS AND PROPHYLAXIS

1260. **Allergy and Immunity in Infants Vaccinated with Large Doses of B.C.G. Given by Mouth According to the Technique of De Assis.** (Allergie et immunité des nourrissons vaccinés par des doses massives de BCG per os selon la technique de De Assis)
E. KRAUS and J. DVORAK. *Presse médicale* [*Presse méd.*] **62**, 1680–1682, Dec. 4, 1954. 1 fig., 15 refs.

In this paper from the General Hospital, Most, Czechoslovakia, the authors discuss the implications of a positive reaction to tuberculin following administration of B.C.G. They do not consider that a reaction to tuberculin is evidence of a satisfactory B.C.G. vaccination, and refer to the work of De Assis, who recommends that after large and repeated doses of B.C.G. immunity should be judged from the reaction to one drop of viable B.C.G. given intradermally. (Another, similar test utilizes killed B.C.G.) The chemical and pathological differences between the tuberculin test and the B.C.G. test are described and discussed.

The authors consider that only infants giving a negative reaction to the B.C.G. test should be vaccinated and that the most effective resistance is found in those negative to the tuberculin test but responding quickly to the B.C.G. test. On the other hand infants with a positive tuberculin reaction and negative B.C.G. reaction are the most likely to develop tuberculosis.

During 1951 and 1952 the authors studied 730 infants vaccinated by mouth with 100 mg. of B.C.G. during the first week of life. Six months after vaccination 45% were allergic to tuberculin and 75% gave a positive reaction to the B.C.G. test; after re-vaccination the latter figure rose to 97%. Fewer than 25% remained tuberculin-negative. Vaccination repeated at monthly intervals resulted in 97% being positive to the B.C.G. test and 90% negative to the tuberculin test after the third month. *T. M. Pollock*

1261. **Experiments on the Lyophilization of B.C.G.** (Essais de lyophilisation du vaccin B.C.G.)
P. HAUDUROY and F. TANNER. *Revue d'immunologie et de thérapie antimicrobienne* [*Rev. Immunol. (Paris)*] **18**, 356–371, 1954. 5 refs.

The authors describe measures designed to test the viability of B.C.G. vaccine freeze-dried by a method devised by the senior author, in which the vaccine is rapidly cooled to −70° C. The technique used is described. Ampoules of lyophilized vaccine were kept at 0° to 5° C., 18° C., 37° C., and 50° C. for 3 years and samples regularly examined. In addition, some were sent and returned by post to addresses in Europe, America, Africa, and Asia. The viability of each sample was then determined by culture studies, estimation of the number of living organisms, post-vaccination skin testing of guinea-pigs, and inoculation of hamsters.

In all samples there was evidence of satisfactory viability, no diminution in the number of living organisms being observed in the vaccine kept at temperatures up to 18° C. during the first 2 years, while samples kept at 37° and 50° C. showed no diminution in viability for periods of 1 year and 8 months respectively. The samples sent by post to various parts of the world showed no diminution in their viability for up to 8 months. Samples of vaccine kept at 18° C. for 6 to 12 months were used to vaccinate a limited number of human subjects; in these Mantoux conversion was observed in over 90%. *T. M. Pollock*

1262. **A Year's Experience of the Vaccination of Young Infants against Tuberculosis by the "Brazilian Method".** (Un an de vaccination antituberculeuse des enfants du premier âge par "la méthode Brésilienne")
D. H. SPARROW, D. M. CARUANA, and G. CARRÉ. *Revue d'immunologie et de thérapie antimicrobienne* [*Rev. Immunol. (Paris)*] **18**, 372–379, 1954. 4 figs.

This paper from the Pasteur Institute, Tunis, describes the results of vaccination of 78 infants in a nursery with massive doses of B.C.G. by the method of De Assis, the so-called "Brazilian method", the infants being given 50 mg. of the vaccine by mouth every 2 weeks until 1 g. in all had been given; they were skin-tested before the first dose and regularly thereafter.

Over 80% became tuberculin-positive after 8 weeks, when 200 mg. had been given, and 99% were tuberculin-positive by 22 weeks. By the 16th week 20% of those with a positive post-vaccination Mantoux reaction had become negative as a result of the repeated doses of the vaccine, and this figure rose to 55% at the end of one year. No adverse symptoms were observed. In one infant bilateral hilar lymph-node enlargement was noted radiologically. *T. M. Pollock*

1263. **Viability and Multiplication of Vaccines in Immunization against Tuberculosis**
H. BLOCH and W. SEGAL. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 228–248, Feb., 1955. 4 figs., 28 refs.

An investigation of the immunizing properties of various antituberculosis vaccines in mice is reported from the Public Health Research Institute of New York City. The survival time of the animals after a challenge infection served as a measure of immunity. In two experiments in which B.C.G. vaccine irradiated for varying periods was used it was found that the degree of immunity conferred was proportional to the number of living cells in the vaccine, but was not significantly affected by the proportion of dead bacilli present. In

another experiment 11 groups of mice (30 in each group) were given isoniazid at intervals of 3 to 24 days after vaccination with B.C.G. and the resistance conferred by the vaccine in the various groups was compared. Survival time was little affected by the interval between vaccination and administration of isoniazid. Assuming that isoniazid inhibits the multiplication of B.C.G. organisms in the mouse, the authors consider the results to indicate that bacterial multiplication is not an essential factor in the production of resistance. In still further experiments a non-multiplying vaccine, H37RA, was found to have immunizing properties equal or superior to those of B.C.G.

In a discussion of the duration of immunity after B.C.G. vaccination it is stated that a crucial rise in immunity occurred after 3 to 6 days, that immunity was highest 3 to 6 weeks later, and that at 9 months there was " little persisting immunity ". *T. M. Pollock*

RESPIRATORY TUBERCULOSIS

1264. **Study of Total Red Cell Volume and Erythrocyte Survival Using Radioactive Chromium in Patients with Advanced Pulmonary Tuberculosis**

J. W. HOLLINGSWORTH and D. R. HOLLINGSWORTH. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 810–815, April, 1955. 3 figs., 13 refs.

Using radioactive chromium (^{51}Cr) the authors, at the Walter Reed Army Medical Center, Washington, D.C., studied the total erythrocyte volume and the erythrocyte survival time in 38 patients with active pulmonary tuberculosis. Anaemia was more common in this group than had been anticipated; because of the relatively low plasma volume in many of the cases the haematocrit value was a poor index of the degree of anaemia. As the authors point out, the possible presence of " masked anaemia " should be borne in mind when major operations are to be performed in such cases. In 2 cases the erythrocyte volume was high, as calculated on the basis of body weight, and the authors suggest the high values were probably related to cachexia.

The life span of the erythrocytes appeared to be normal, but the erythrocyte survival curve for females was slightly shorter than that for males. *J. B. Wilson*

1265. **Preliminary Results of Electrophoresis of the Plasma Proteins and Lipids in Pulmonary Tuberculosis.** (Premiers résultats de l'électrophorèse des protides et des lipides dans la tuberculose pulmonaire)

A. MEYER, H. KAUFMANN, and J. GELIN. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **19**, 178–186, 1955. 6 figs., 13 refs.

The protein pattern in 110 samples of plasma from 88 patients and the lipid pattern in those from 45 patients with pulmonary tuberculosis at the Boucicaut and Broussais Hospitals and the Hôtel-Dieu, Paris, were examined by paper electrophoresis. It was found that the plasma samples could be divided into four groups according to the protein distribution, these showing respectively increased α_2-globulin value (28 cases), increased β-globulin value (10 cases), increased γ-globulin value (12 cases), and normal electrophoretic pattern (19 cases). On correlation with the clinical status of the patients these findings seem to suggest that a persistently high α_2-globulin value is associated with a poor prognosis and a high γ-globulin value with an old lesion. The finding of a low lipid value was suggestive of an active state of the disease, but the results of the lipid determinations were difficult to interpret, the separation of different fractions being insufficient to permit of any conclusions being reached. (It is emphasized that these observations are of a preliminary nature and that the suggestions as to clinical significance should be treated with reserve.) *J. E. Page*

1266. **Disturbances of the Plasma Proteins in the Course of Pulmonary Tuberculosis.** (La perturbation des protéines du plasma au cours de la tuberculose pulmonaire)

B. KREIS, M. F. JAYLE, P. CLERC, and H. LUTIER. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **19**, 187–196, 1955. 26 refs.

In an investigation of the significance of disturbances of the plasma protein pattern in tuberculosis 48 samples of plasma from patients with pulmonary tuberculosis were examined both by paper electrophoresis and by a series of standard chemical tests, and the results compared. Electrophoresis gave good general information on all the proteins, whereas the chemical tests gave more specific information on individual protein fractions. The total plasma protein and fibrinogen content, however, could be determined only by chemical tests. It was shown that during the course of pulmonary tuberculosis a rise in the α_2-globulin value—causing a rise in the haptoglobin index—and in γ-globulin, fibrinogen, and sometimes β-globulin values occurred. The rises were, however, slight and inconstant and are considered unsuitable as an aid to either clinical diagnosis or prognosis. They could not be relied on to indicate when treatment should be stopped. *J. E. Page*

1267. **Observations on the Pathogenicity of Isoniazid-resistant Mutants of Tubercle Bacilli for Tuberculous Patients**

R. OESTREICHER, S. H. DRESSLER, W. F. RUSSELL, J. B. GROW, and G. MIDDLEBROOK. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 390–405, March, 1955. 25 refs.

Observations are reported from the National Jewish Hospital, Denver, Colorado, of the effect of isoniazid alone in the treatment of 45 patients suffering from advanced pulmonary tuberculosis who had a persistently positive sputum containing isoniazid-resistant organisms. The drug was given in a daily dosage of 4 to 16 mg. per kg. body weight (generally 8 mg. per kg.) for periods of 6 to 25 months (average one year). Unless there was clinical evidence of toxicity the patients were not confined to bed. Tests of sputum cultures revealed that the organisms were catalase-negative in 25 cases and catalase-positive in 17; in one case the catalase test was not performed and in 2 catalase-negative organisms were found during the early period of the investigation and

mixed cultures with some catalase-positive organisms later. It is of interest that the 17 patients with catalase-positive bacilli in the sputum fared as well as those with catalase-negative bacilli. Four patients gained 10% or more in weight during the period of treatment, 9 lost 10% or more, and 32 remained unchanged. A rise in temperature for brief periods in 8 cases was unaffected by administration of penicillin, erythromycin, or tetracycline; in 6 cases there was slight to moderate pulmonary haemorrhage.

Radiologically, no significant change was observed in 32 patients, but marked improvement was noted in 2. In 11 cases the condition was worse, there being progressive enlargement of the cavities with thinning of the walls in 4 cases, transient infiltrations, clearing completely in a few weeks, in 4, new shadows in 2, and interlobar pleural effusion in one.

The authors differentiate mechanical atelectasis and "epituberculosis" from true bronchogenic spread, and consider that, with the possible exception of one case, bronchogenic spread did not occur in their series. They also point out that no complication such as tuberculous meningitis or laryngitis was encountered. They consider that bacilli which are deficient in endogenous catalase activity simultaneously lose pathogenicity and are not capable of causing spread in healthy tissues. Further, isoniazid in adequate dosage inhibits multiplication of drug-susceptible organisms and bacilli resistant to this drug "suffer genetic loss of a physiologic function which is essential for [their] full pathogenicity". *G. M. Little*

1268. **Intermittent Treatment with Isoniazid.** (Intermittierende INH-Behandlung)
I. Seri, E. Fehérvári, and I. Szabó. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **113**, 234–240, 1955. 1 fig., 10 refs.

Following experiments on mice, which are briefly described, the authors investigated the effect of the intermittent administration of isoniazid to an unselected group of 60 patients, all suffering from subacute pulmonary tuberculosis, in most cases with fibro-caseous lesions, and considered to be in need of prolonged chemotherapy, who were admitted during one year to the Korányi Sanatorium, Budapest. A comparable group of 50 patients in a similar stage of the disease were given isoniazid daily and served as a control group. The experimental group received 10 mg. of isoniazid per kg. body weight and 10 to 16 g. of PAS daily for 3 days and then had 4 days' rest; the control group were given 5 mg. of isoniazid per kg. and 4 to 12 g. of PAS every day, treatment of both groups being continued for 16 to 18 weeks. It is noted that both groups had also received 2 weeks' continuous isoniazid therapy before entering the sanatorium.

The results were assessed in terms of clinical improvement [although clinical details for the control group are lacking], on improvement in the radiological appearances and erythrocyte sedimentation rate, on examination of sputum films and cultures, and by determination of sensitivity of the causal organism to isoniazid. Over the period under review patients receiving intermittent therapy did slightly better in all respects than those in the control group. There was no evidence of increased liability to the development of drug resistance. Two patients who had failed to respond to the daily administration of isoniazid because of the development of resistance showed marked improvement in response to the intermittent therapy. *P. Mestitz*

1269. **The Intravenous Administration of PAS in the Combined Treatment of Pulmonary Tuberculosis.** (Le perfusioni endovenose di PAS nel trattamento combinato della tubercolosi polmonare)
M. Reale, S. Ferro, and A. Garaventa. *Riforma medica* [*Rif. med.*] **69**, 509–518, May 7, 1955. 21 refs.

The authors report from the Maragliano Sanatorium, Genoa, the results of the treatment of 59 patients in various stages of pulmonary tuberculosis by the intravenous infusion of PAS alone (9 cases), or in combination with the administration of streptomycin or isoniazid (9 cases), or with all three drugs together (41 cases). The infusion was prepared by dissolving 15 g. of PAS in 500 ml. of a stabilized, non-pyrogenic, and non-irritant solution described by Douris and Bory [no reference given] and administered intravenously drop by drop over 2 to 3 hours every third day for 2 to 4 weeks. Toxic symptoms, which were observed in less than 10% of the patients, consisted mainly in gastro-intestinal disturbances, with diarrhoea and some rise of temperature.

The intravenous infusion of PAS alone did not produce satisfactory results. But the combination of this treatment with intramuscular injections of 1 g. of streptomycin every third day or the administration of isoniazid by mouth (100 mg. twice daily) on the two intermediate days resulted in considerable improvement. The length of treatment was dependent upon the gravity of the case; the administration of PAS and isoniazid was usually continued for another year as a prophylactic measure to prevent relapse. *Franz Heimann*

1270. **The Long-term Results of the Treatment of Giant Cavities of the Lung with Surgical Extrapleural Pneumothorax.** (I risultati a distanza del trattamento delle caverne giganti del polmone con il pneumotorace extrapleurico chirurgico)
G. Capaldo and V. Gualtieri. *Rivista della tubercolosi e delle malattie dell'apparato respiratorio* [*Riv. Tuberc.*] **3**, 36–50, Jan.–Feb., 1955. 9 figs., 9 refs.

The authors, writing from the Carlo Forlanini Institute, Rome, discuss the long-term results of extrapleural pneumothorax performed on 54 patients with giant tuberculous cavities. The cases were divided into two groups: (1) those in which the pleura was wholly or partially free, and (2) those in which it was totally adherent.

In the first group extrapleural pneumothorax was imposed on an inefficient intrapleural pneumothorax. Of 30 such cases, the long-term results were satisfactory in 20, 5 patients died, and 5 were lost to follow-up. In the second group, primary extrapleural pneumothorax was performed on 24 patients, of whom 18 did well on follow-up and 6 died. Thus of the total of

54 patients, 38 (70%) had apparently arrested disease at follow-up examination, 11 (20%) died (9 from tuberculosis and 2 from non-tuberculous causes), and 5 were lost sight of. As to complications, broncho-pleural fistula occurred in 4 patients, of whom 3 died and one is dying, bronchogenic spread of the disease to the contralateral side in 4 patients, of whom 3 died, and in 6 cases pyogenic, mixed, or tuberculous empyemata developed. [These cases seem to have been treated between 1947 and 1951, giving a minimum follow-up period of 3 years.]

The authors state that 21 (38·7%) of the pneumothoraces have been abandoned and 17 (31·4%) are in process of abandonment. Despite the alarming total collapse of the lung in 3 cases, described in detail, the authors claim that they had no difficulty in obtaining terminal lung expansion. [The periods of maintenance of the pneumothorax are not stated, nor is there any mention of chemotherapy.] The authors admit on reflection that many of these cases would have been preferably treated by resection at the present time. But they maintain that in those cases in which the disease is widespread and resection is therefore contraindicated, extrapleural pneumothorax has a place.

[Despite the results obtained it must be mentioned that many members of the staff of the Forlanini Institute consider the induction of extrapleural pneumothorax in cases of such advanced disease to be inadvisable, as tending to bring the procedure into disrepute, unless the cavities have been reduced to a comparatively small size preoperatively by previous chemotherapy.]

Arnold Pines

1271. **Bilateral Surgical Extrapleural Pneumothorax.** (Alcune considerazioni sul pneumotorace extrapleurico chirurgico bilaterale)

A. Monaco and C. Roscioni. *Rivista della tubercolosi e delle malattie dell'apparato respiratorio* [*Riv. Tuberc.*] 3, 51–80, Jan.–Feb., 1955. 1 fig., 18 refs.

The authors review the place of bilateral extrapleural pneumothorax in the treatment of pulmonary tuberculosis and discuss the results in 22 patients so treated at the Carlo Forlanini Institute, Rome. They consider that the procedure is indicated in cases of bilateral upper-lobe disease preferably affecting the apical or posterior segments, and in cases of minimal or moderately advanced disease without giant cavities, manifest endobronchitis, or extensive fibrosis. They restrict the operation to patients under 40 years of age (1) when respiratory and cardiovascular tests show comparatively little impairment of these functions, (2) when the toxicity and acuteness of the lesions have subsided, and (3) when intrapleural pneumothorax has failed, as is usually the case.

Of their 22 patients, 14 did well, 6 derived moderate benefit only, and in 2 the results were bad. These last 8 patients had disease in the middle zones [the precise lobes are not defined] or had giant cavities. Most patients showed little or no respiratory impairment on examination by bronchospirometric and oxymetric tests repeated after the operation, although in order to attain this preservation of function the authors emphasize that refills must not be large. The interval between induction of pneumothorax on the two sides of the chest was 3 to 5 months, although sometimes after the more affected side had been treated initially the contralateral lesion improved remarkably, and operation was therefore deferred until this improvement had reached its maximum. These cases were treated between 1943 and 1953, the majority after 1950, so that in the latter the follow-up period was short and in many cases the pneumothorax had not yet been abandoned. In those in which it had been given up there were no serious complications.

[Chemotherapy was archaically restricted to some 20 days before operation and for a short (variable) period after it, the authors defending this on the grounds of the risk, rather exaggerated, of producing drug resistance. These short courses had, nevertheless, almost eliminated serious infective complications of the operation due to the tubercle bacillus.]

Arnold Pines

1272. **Resection Failures in Pulmonary Tuberculosis**

R. J. Schlosser and F. J. Jarvis. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **29**, 335–343, April, 1955. 2 figs., 10 refs.

Between June, 1946, and September, 1951, at Firland Sanatorium, Seattle, pulmonary resection was performed on 400 patients suffering from tuberculosis (411 resections), and in this paper the authors examine the reasons for failure of this operation in 54 cases. The resection procedures included pneumonectomy (160), lobectomy (244), segmental resection (6), and " nodulectomy " (1). In all but the first 38 cases streptomycin was given in a dosage of 1 g. daily, usually for 1 to 14 days before operation and for 2 to 6 weeks afterwards. Patients were kept in bed for a minimum of 6 months following operation and most were discharged at the end of one year. Of the 400 patients, 21 died within 6 weeks of operation—14 after pneumonectomy (8·7%) and 7 (2·9%) after lobectomy. There were 33 late deaths (6 weeks or more after operation) from complications " for the most part directly related to surgery ". A total of 27 patients had to be readmitted for further treatment, more than half of them within 2 years and the remainder over a period of 4 to 6 years. In all of these there was evidence of reactivation or spread of the disease on *x*-ray or sputum examination.

A follow-up assessment in 357 of the 400 cases revealed that a good result had been achieved in 279, the patient being well and the sputum negative. The authors state that inadequate respiratory reserve was the major cause of both early and late deaths in the series and that in many of the cases of pneumonectomy more conservative resection would have been performed but for technical difficulties at the time of operation. The importance of obliterating any residual pleural space because of the risk of the development of a late broncho-pleural fistula is emphasized. At operation every attempt should be made to remove all residual caseous foci.

A. M. Macarthur

See also Pathology, Abstract 1205.

Venereal Diseases

1273. **Susceptibility of *Neisseria gonorrhoeae* to Eleven Antibiotics and Sulfadiazine. Comparison of Susceptibility of Recently Isolated Strains with Results Obtained in Previous Years in the Same Laboratory**
B. DEL LOVE and M. FINLAND. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 66–73, Jan., 1955. 1 fig., 39 refs.

The sensitivity of 108 strains of *Neisseria gonorrhoeae* to 11 antibiotics and to sulphadiazine was studied at the Thorndike Memorial Laboratory and Harvard Medical School, Boston. Penicillin was the most effective of the agents tested and erythromycin, though considerably less active, came next; the remainder in order of sensitivity were oxytetracycline, tetracycline, chlortetracycline (aureomycin), chloramphenicol, carbomycin, streptomycin, neomycin, bacitracin, sulphadiazine, and polymixin B.

A comparison of these findings with those of a similar investigation carried out in 1949 did not reveal any significant change in the sensitivity of the organisms to penicillin. The authors state that any slight changes observed were well within the range of variability in the purity of the preparation used and the limits of experimental error in the method, which involved the inoculation of the organism on a series of agar plates containing doubling dilutions of the antibiotic. The percentage of strains resistant to sulphadiazine in a concentration of 100 μg. per ml. was 84 in 1949 compared with 19 in the present investigation; this is attributed to marked decrease in the use of sulphonamides in the treatment of gonococcal infection. *John M. Talbot*

1274. **Notes on the Treatment of Nongonococcal Urethritis in Males with Tetracycline**
B. G. CLARKE, H. CHAIMSON, H. GOLDEN, and H. N. TASHIAN. *Bulletin of Tufts–New England Medical Center* [*Bull. Tufts–New Engl. med. Cent.*] **1**, 34–36, Jan.–March, 1955. 5 refs.

Results are reported from the Boston Dispensary of the treatment with tetracycline of 16 males suffering from non-gonococcal urethritis. The drug was given by mouth in doses of 250 mg. 4 times daily for 5 days. In all cases the urethral discharge disappeared within 1 to 5 days of the start of treatment and did not recur during the period of observation, which lasted from 1 to 3 weeks. No untoward reactions to the drug were observed.

The incubation period in these cases varied from 2 to 42 days. From cultures of the discharge made in 13 cases *Staphylococcus albus* was isolated. Of 10 strains of this organism tested, 9 were sensitive to tetracycline *in vitro*; however, the one patient with resistant organisms responded clinically. Five of 6 tetracycline-sensitive strains of *Staph. albus* were found to be resistant to sulphonamides.

A further 6 patients with a non-gonococcal urethral discharge associated with prostatitis were also treated with tetracycline. The urethral discharge ceased in all 6 cases, though 2 cases later relapsed owing to the emergence of organisms resistant to the antibiotic.
R. R. Willcox

1275. **Effect of Room Temperature on Serologic Tests for Syphilis**
H. N. BOSSAK, A. HARRIS, and S. OLANSKY. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 33–36, March, 1955. 6 refs.

As "room temperature" is subject to wide seasonal and regional variations, the authors, at the Venereal Disease Research Laboratory, Chamblee, Georgia, carried out a block of serological tests for syphilis in triplicate at various temperatures. The tests were: Kahn with lipoid antigen, Kline, Mazzini, Rein–Bossak, V.D.R.L. slide and tube tests—in all of which cardiolipin–lecithin antigens were used. The temperatures ranged from 15° C. over 21°, 23°, 25°, 27°, 29°, and 32° to 40° C.

The results, presented in tables, are discussed for the 4 slide flocculation tests (V.D.R.L. and Kahn are considered separately). Reactivity in both qualitative tests and quantitative tests was found to increase with increasing temperature between 15° and 40° C. An attempt was made to define a temperature range within which no gross change in reactivity would occur, and this was found to be between 23° and 29° C. The V.D.R.L. tube test showed no significant variation in reactivity over the whole range. With the Kahn test, reactivity did not appear to change much between 15° and 25° C., but fell at 40° C.; also in the range 21° to 32° C. the results did not vary, so that 23° to 29° C. (73° to 84° F.) appears to be the optimum temperature for all tests. *F. Hillman*

1276. **VDRL Slide Flocculation Reaction for Syphilis Performed on Active Sera**
E. E. SCHMID and T. VELAUDAPILLAI. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 37–39, March, 1955. 15 refs.

The authors, at the Medical Research Institute at Colombo, have modified the V.D.R.L. slide flocculation test so as to render inactivation of the serum unnecessary. (Active sera are also used for the Meinicke and citochol flocculation reactions, but not a chemically defined antigen.) After being stabilized by the addition of hypertonic saline solution active sera were tested by the modified technique and parallel tests carried out on the same but inactivated sera by the original technique.

The modifications of technique are briefly outlined and the crucially important preparation of antigen emulsion is described in detail. The antigen was found

to be stable for 4 days when stored at +4° C. All measurements are made with 56 Starret-gauge pipettes.

The results of 15,000 double tests are compared in a table and shown to agree with a statistically non-significant error. The percentage agreement between the two tests was 98·29%, but a large number of non-reacting sera contributed to this high agreement; among reacting sera the agreement was 86·01%. *F. Hillman*

1277. **Comparison of the Ide and Harris (VDRL) Slide Flocculation Tests in Nigeria**

L. R. BOULGER and D. A. CANNON. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 40–43, March, 1955. 5 refs.

The authors, from the Laboratory Headquarters, Yaba, Nigeria, present the results of a comparison of the Ide and Harris (V.D.R.L.) slide flocculation tests for syphilis and yaws, in which the standard 3-tube Kahn test was used as a basis. A total of 8,077 sera from Nigerian subjects were tested. The Ide test was modified by the use of inactivated serum instead of whole bood, and the 2·5% sodium chloride solution used to suspend the antigen was buffered to *p*H 6·1.

The results of the Ide and Harris tests were found to agree quite well with those of the Kahn test, the comparison slightly favouring the Harris test. It was also found that with both tests the positive results could be subdivided into weakly and strongly positive, but as the clinical details were inadequate it was not possible to correlate this with clinical findings. In comparison with the Kahn test, however, this subdivision favoured the Harris test significantly (χ^2=43·3156).

In sera from 3,468 patients with "some" evidence of syphilis or yaws the Harris test was significantly more sensitive, and with the division of positive reactions into weak and strong the Harris test became even more significantly superior. Again the two tests agreed well on a group of sera from 3,404 patients giving no history or evidence of syphilis or yaws, but when regarded on the basis of weak and strong positive results the Harris test proved significantly more specific. An additional advantage of the Harris test is that the antigen can be stored for 24 hours, whereas the Ide antigen must be used within 10 minutes of its preparation. This is partly offset, however, by the costliness of the Harris as compared with the Ide antigen. *F. Hillman*

1278. **Yaws in Manchester**

S. M. LAIRD. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 30–32, March, 1955. 3 refs.

In briefly reviewing present knowledge regarding yaws the author points out that the disease occurs in tropical and sub-tropical areas where syphilis is rare. He then comments on the considerable influx of West African and West Indian males into England in the last few years, and states that these men present a medico-social problem, since they form a significant proportion of infected patients attending venereal disease clinics [no actual figures are given], where it has been found they have positive serological reactions to tests for syphilis with greater frequency than the native population of England. The author suggests the possibility that many of these positive reactions to the Wassermann and Kahn tests may be due not to syphilis, but to yaws. The importance of arriving at a clear differentiation between late yaws and latent syphilis is discussed at some length.

The author then describes a study, at Manchester University, of 48 coloured patients (42 of them from West Africa or the West Indies), of whom 34 had attended initially for treatment for gonorrhoea or non-gonococcal urethritis. Examination revealed residual evidence in the skin or bones of past infection with yaws in 26 patients, 11 of whom were aware of having had the disease. Evidence suggestive of yaws was present in several others, although the diagnosis could not be confirmed. A case of yaws in a white child is also reported.

[This article reflects the widened outlook in British venereology, namely, that treponematosis should be considered as a group of diseases rather than in terms of syphilis alone.] *R. S. Morton*

1279. **Topical Cortisone in Syphilitic Interstitial Keratitis. Review of Twenty-three Cases (29 Eyes)**

G. O. HORNE. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 9–24, March, 1955. 31 refs.

After deploring the reluctance to use topical cortisone in the treatment of syphilitic interstitial keratitis, which is due in part to conflicting reports in the literature regarding its efficacy and in part to an exaggerated fear of its side-effects, the author goes on to discuss the effects of cortisone on the manifestations of the condition, with special reference to the duration of the attack, incidence of relapse and recurrence, ultimate visual acuity, and involvement of the other eye, as seen in 23 patients (29 eyes) treated at the General Infirmary at Leeds with a suspension in normal saline of cortisone acetate in a concentration of 5 mg. per ml. The patients were given one drop in the affected eye at intervals of one to 4 hours—the more severe the condition, the more frequent the treatment—this being continued day and night if necessary for the first few days. Once the condition was under control, treatment was restricted to 4-hourly applications during the day only. It is stressed that care must be taken not to stop therapy suddenly and prematurely, which may cause a relapse. Where this occurred it was promptly controlled by further topical application of cortisone.

The author points out that the best early results were obtained in patients who were admitted to hospital for their initial treatment, and that the earlier the initial treatment, the more is it likely that permanent damage, in the form of impaired acuity, will be prevented. If cortisone is not administered until infiltration and vascularization have occurred the outcome is less certain, although still reasonably good. There is no evidence that the use of cortisone prolongs the interstitial keratitis or increases the likelihood of relapse, nor that harm can result from using too high a dosage over a short time. The author concludes by expressing the opinion that failure to use cortisone in the treatment of interstitial keratitis is tantamount to neglect. *R. S. Morton*

Tropical Medicine

1280. **Encephalitis following Neurotropic Yellow Fever Vaccine Administered by Scarification in Nigeria: Epidemiological and Laboratory Studies**
P. B. STONES and F. N. MACNAMARA. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **49**, 176–186, March, 1955. 1 fig., 16 refs.

During an outbreak of yellow fever in Eastern Nigeria 42,400 inhabitants of the township of Enugu were vaccinated between January 14 and February 9, 1952, with a neurotropic yellow-fever vaccine from the Pasteur Institute, Dakar, the intradermal scarification method being used. Between January 28 and February 21, 1952, 83 cases of encephalitis were admitted to Enugu Hospital and 32 deaths ensued, 73 of these cases, with 29 deaths, being in children under 10 years of age. Of the 3 different batches of vaccine used, all appeared to be equally implicated.

Carefully controlled specificity tests of the 3 types of virus recovered from the brains of victims proved them to be neurotropic yellow-fever virus. Investigation of the potency of the vaccine showed the production of antibodies in 90% of the population inoculated. In view of the rarity of encephalitis after the use of this vaccine either in French West Africa or the Gold Coast, where vaccinia virus is generally inoculated simultaneously, it is suggested that possibly this combination may minimize the risk.

The authors conclude: " In spite of accidents such as we have reported, there can be no doubt that both the mouse-brain and 17D vaccines have been of vast benefit to mankind. . . . It remains to study further in what way the disadvantages of each can be eliminated and their advantages combined ". *Clement C. Chesterman*

1281. **Tuberculin and Lepromin Sensitivity in the South African Bantu. A Pilot Survey**
S. W. A. KUPER. *Lancet* [*Lancet*] **1**, 996–1001, May 14, 1955. 3 figs., 16 refs.

From the statement frequently made that skin sensitivity to tuberculin and that to lepromin are correlated it has been inferred that an immunological relationship exists between the two substances. To elucidate this problem 57 patients with pulmonary tuberculosis, 52 with lepromatous and 50 with tuberculoid leprosy, and 105 healthy controls were more or less simultaneously inoculated with (*a*) tuberculin and (*b*) a lepromin tending to produce more prominent early acute reactions (and so more comparable with tuberculin). A significant correlation between tuberculin and lepromin sensitivities was observed only in the patients with pulmonary tuberculosis; there was none in the controls or in the 85 adult patients with leprosy. Sensitivity to tuberculin differed greatly in the two forms of leprosy, and less strong reactions were obtained in the tuberculoid form (particularly in males) than in the control group. Patients with pulmonary tuberculosis were more sensitive to lepromin than the controls.

It is concluded that the relationship between tuberculin and lepromin sensitivities is not a simple and direct one. *R. Crawford*

1282. **The Treatment of Amoebic Colitis with Antibiotics.** (La terapia antibiotica della colite amebica)
V. PINTO and C. PEZZULLO. *Acta medica Italica di malattie infettive e parassitarie* [*Acta med. ital. Mal. infett.*] **10**, 1–12, Jan., 1955. Bibliography.

After a discussion of the use of various antibiotics in the treatment of amoebiasis the authors describe in detail the results of treatment of 10 cases of this disease in adults with fumagillin at the University Clinic for Infectious and Tropical Diseases, Naples. In all cases the diagnosis was confirmed microscopically. Most of the patients were suffering from active dysentery, but in 2 cases cysts only were present. The dosage of fumagillin given was 60 mg. daily divided in three doses (7 patients), 40 mg. daily (2 patients), or 30 mg. daily (1 patient) over periods of 12 to 20 days.

Side-effects occurred in most cases, the commonest reaction being anorexia (6 patients). Mild hypotension developed in 2 patients, and severe hypotension (blood pressure 95/60 mm. Hg) in one patient, who also suffered from diarrhoea, tenesmus, nausea, and abdominal pain severe enough for treatment to be stopped. Of the other 9 patients, 8 responded rapidly to treatment; the 9th was suffering from rectal polyps and responded less satisfactorily. A follow-up examination of 7 patients showed that only 3 had relapsed within 2 months; the others were observed from 2 to 14 months, and were still well. *W. H. Horner Andrews*

1283. **Amebiasis: Controlled Linear Studies on Non-dysenteric and Mild Hepatic Forms in Egyptians**
H. L. JONES, G. CASSIS, T. M. FLOYD, and N. S. MANSOUR. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 763–785, April, 1955. 10 figs., bibliography.

To test the occurrence of non-dysenteric and mild hepatic forms of amoebiasis among symptomless or " healthy " carriers of *Entamoeba histolytica* the authors investigated 19 apparently healthy Egyptian employees of a U.S. Naval Medical Research Unit in Cairo. These were examined physically every week, and a daily record was kept by the subjects themselves of the number of stools passed together with the occurrence of gastro-intestinal symptoms such as flatulence and abdominal cramps. Stools were examined weekly. After 24 weeks all subjects who had passed *E. histolytica* were treated with " vioform " (iodochlorhydroxyquinum) and carbazone; when hepatitis was suspected chloroquine was also given. Physical and stool examinations were continued for a

further 24 weeks on 18 of the subjects and also on another 5 similarly treated.

Three groups were identified before treatment: Group I (10 subjects) at one time or another passed both large and small races of amoebae; Group II (5 subjects) harboured the small race only; and Group III (4 subjects) had persistently negative stools. The last group served as a control. After treatment, subjects cured were added to Group III. There was no real difference between the three groups in the number of stools passed per day, but soft stools were far more frequent in Group I. Frequency of symptoms was again commonest in Group I, but that of signs (tenderness of large intestine and liver) was about equal in Groups I and II and far greater than in controls. Successful treatment reduced the frequency of abnormalities to the control level. Of the combined total of 23 subjects, 11 remained negative in the post-treatment period.

The authors conclude that the small race of amoebae (trophozoites, 12 μ; cysts, 9·6 μ) are mildly pathogenic, and that " apparently healthy carriers " of either small or large race of micro-organism may show mild signs and symptoms of amoebiasis if observed over a long enough period. *W. H. Horner Andrews*

1284 (*a*). **Non-suppurative Intrathoracic Complications of Amoebiasis.** (Les complications intra-thoraciques non suppurées de l'amibiase)

1284 (*b*). **The Suppurative Intrathoracic Manifestations of Amoebiasis.** (Les manifestations suppurées intra-thoraciques de l'amibiase)

1284 (*c*). **Amoebic Pericarditis.** (Les péricardites amibiennes)

R. Coirault, H. Coudreau, and J. Girard. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 1591–1602, 1603–1617, and 1617–1621, May 6, 1955. 42 figs., bibliography.

In the first of these three papers the authors describe 20 cases of amoebiasis exhibiting non-suppurative intra-thoracic complications in patients, including members of the French Expeditionary Force in Indo-China, who had all been exposed to infection in the tropics. They suggest that such cases can be divided into three groups. (1) In the first group there is diffuse involvement of the lung and pleura at the right base which, pathologically, is an extension by contiguity of an amoebic hepatitis, though clinically the main presenting symptom may be a painful cough. Radiography shows a diffuse shadow at the right base, with elevation of the diaphragm and a thickening of the lower end of the interlobar fissure. (2) Cases in the second group present with pneumonitis or discrete disseminated foci of infiltration. Clinically the onset may be sudden or subacute; in some cases haemoptysis may occur. (3) In the third group the first sign is pleural effusion. In these cases the leucocyte count may be normal or moderately increased, and aspirated pleural fluid may show a preponderance of lymphocytes in the exudate. In such cases the authors consider that the pleurisy is a " reaction at a distance " to the amoebic infection. They describe in some detail a chronic case of the third type in which the patient had returned from active service in Indo-China 15 years previously. The history and clinical signs pointed strongly to a tuberculous effusion, but inoculation of the aspirated fluid into guinea-pigs gave negative results. Aspirated pleural fluid showed a preponderance of lymphocytes although the leucocyte count in the blood was normal. The liver was neither enlarged nor tender on palpation. Examination of the stools showed amoebae containing ingested erythrocytes. Radiological examination revealed immobility and slight elevation of the right cupola of the diaphragm. Finally, the administration of emetine was followed by excellent results.

An important point in the diagnosis of these cases is a history of possible exposure to infection, such as by residence in an endemic area, or of previous attacks of dysentery or diarrhoea. Radiological signs include elevation, paralysis, and " peaking " of the right cupola of the diaphragm. The authors stress the value of a sign consisting in thickening of the lower end of the interlobar fissure on the right side. The final criterion of diagnosis in most of their cases was not the presence of amoebae in the stools, but the therapeutic response to emetine in those cases in which the epidemiological, clinical, and radiological findings pointed to amoebic infection.

In their second paper the authors present observations in 19 cases of amoebiasis complicated by intrathoracic suppuration. These fell into two groups, the first of which included 6 cases of hepato-bronchial fistula in which the diagnosis was comparatively straightforward, the characteristic chocolate-coloured pus being coughed up in profuse quantities. Confirmatory radiological and clinical signs were present at the base of the right lung. The authors then describe 4 cases in which the lung abscess was not in direct anatomical communication with the hepatic suppuration. Here they had to rely more on the history of amoebiasis or exposure to infection, the nature of the pus, and the response to treatment. There must always be considerable doubt about the aetiology of such abscesses, but the authors give a full account of the considerations on which they based their diagnosis, stressing the value of the observation that in such cases the magnitude of the pulmonary lesions is insufficient to account for the symptoms. The presence of leucocytosis helps to differentiate the condition from pulmonary tuberculosis, and the diagnosis can be confirmed by examination of aspirated bronchial fluid.

The authors' second group consisted of 7 cases of amoebic pyothorax due to rupture of a hepatic abscess into the pleural cavity. This is one of the most serious complications of amoebiasis; if adhesions have already formed near the site of rupture the empyema may be localized, but if there are no adhesions the whole pleural cavity is open to contamination, which may result in the subsequent development of pyopneumothorax. Three possible types of fistula can occur, namely, hepato-pleural, hepato-bronchial, and broncho-pleural, and in one of their cases the authors observed the successive development of all three. When the empyema is localized the onset may be insidious, but in the absence of adhesions it is always dramatic and accompanied by severe symptoms. The right pleural cavity is the more commonly

involved, but the authors have observed rupture into the left pleural cavity from an abscess in the left hepatic lobe. In some cases the complication develops during the course of treatment of hepatic abscess, and then the diagnosis is comparatively easy. Difficulty arises when the first sign is an empyema or pyo-pneumothorax. They consider that in the aetiology of intrathoracic suppuration associated with amoebiasis direct extension from a hepatitis resulting in a localized empyema or broncho-hepatic fistula is far more common than an isolated amoebic abscess of the lung.

In the last of these three papers the authors describe a case of rupture of an abscess into the pericardial sac—a rare complication of amoebic hepatitis. The literature is briefly reviewed. The patient was a known alcoholic who had been repatriated from active service in Indo-China with a diagnosis of hepatic cirrhosis. After a short stay in hospital, during which a painless hepatomegaly was noted, he discharged himself, but was re-admitted 3 months later in a cachectic state. He had then continuous fever, gross enlargement of the liver and spleen, and a leucocytosis of 11,000 cells per c.mm., of which 56% were polymorphonuclear. A pericardial rub was present and radiographs showed an increase in size of the cardiac shadow. Pericardial aspiration was attempted but no fluid could be obtained. No malarial parasites were found in the blood, and only non-pathogenic amoebae were present in the stools. Penicillin, chloroquine, streptomycin, PAS, and salicylates were successively prescribed with doubtful effect on the fever and with no effect on the pericarditis. About the tenth week there was a dramatic deterioration in the patient's condition, when he developed clinical signs of pneumothorax and aspiration revealed a chocolate-coloured fluid. The therapeutic response to emetine was rapid, and the patient made a reasonably good recovery for a time, which was, however, gravely compromised by his continued intemperance.

William Hughes

1285. **Immunity to Reinfection following Recovery from Cutaneous Leishmaniasis (Oriental Sore)**

F. SAGHER, S. VERBI, and A. ZUCKERMAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 417–421, April, 1955. 12 refs.

As inhabitants of endemic areas do not usually suffer more than once from oriental sore, it has been generally assumed that patients recovering from this disease possess a lasting immunity to infection. This theory was tested at the Hebrew University–Hadassah Medical School, Jerusalem, by attempting to reinfect 9 subjects in whom infection with *Leishmania tropica* had been induced experimentally and 7 who had been infected naturally in childhood. The 9 subjects who had not previously been naturally infected each received a subcutaneous inoculation of 1,000,000 leptomonads grown in a medium containing agar, Locke's solution, and rabbit serum. Typical lesions of early cutaneous leishmaniasis developed at the inoculation sites. Leishmanin reactions, which were negative before inoculation, became positive during development of the lesion. In all but one case positive cultures were obtained from the sores.

Clinical healing was observed in these subjects 6 to 17 months after inoculation, following which cultures and microscopical examination of material aspirated from the scar were negative for *Leishmania*. These subjects were reinoculated with 1 to 5 million culture flagellates from the same strain as that employed to induce the primary lesion, as were the 7 subjects who had been infected with leishmaniasis during childhood. In none was a successful reinfection obtained, although a typical accelerated reaction corresponding to the second part of Koch's fundamental experiment in tuberculosis was noted. The results are held to confirm that patients recovering from cutaneous leishmaniasis are generally resistant to reinfection with *L. tropica*. *R. R. Wilcox*

1286. **The Importance of Microscopic Granulomas (Pseudotubercles) in the Diagnosis of Manson's Schistosomiasis**

O. F. DEGOUVEIA and W. D. BEAMER. *Gastroenterology* [*Gastroenterology*] **28**, 634–641, April, 1955. 4 figs., 9 refs.

In recent years there has been an influx into the U.S.A. of natives of Puerto Rico, where *Schistosoma mansoni* infection is highly endemic. While there is at present no evidence that infected individuals serve to spread schistosomiasis in the United States, diagnosis of the disease is of importance to the patient concerned. With this in view all natives of Puerto Rico admitted to the Gastrointestinal Clinic of the Jefferson Hospital, Philadelphia, between September, 1953, and July, 1954, were examined proctoscopically, biopsy specimens being taken from the superficial mucosa of the rectal valves, and the results are now presented. Of the 62 cases concerned, cultures were positive for *S. mansoni* in 3. In 13 of these cases single or multiple granulomata were present; 4 had granulomata only, and in the remainder eggs were found in addition without extensive tissue reaction. In 9 of these granulomatous cases the rectal mucosa appeared normal. Eggs only, without granulomata, were found in 10 cases.

Granulomata in the early stages consisted of a zone of lymphocytes, eosinophil granulocytes, and monocytes, with epithelial and giant cells, concentrically enclosed in fibroblasts. Schistosome eggs were centrally situated in most cases. Older granulomata were largely replaced by a fibrous nodule which could be flattened out in the unstained biopsy material and distinguished under the low power of the microscope. The authors point out that at this stage eggs or remnants of them are not always to be seen, but staining with Lugol's iodine may help to identify them. In only 2 instances were histological sections from 7 positive cases reported to be positive for *S. mansoni*.

The authors consider that granulomata without identifiable eggs should be regarded with suspicion and as indicating the need for further search. In the present series viable eggs were not recovered from any granulomata. *B. G. Maegraith*

Allergy

1287. **Prevention of Bronchial Reactions to Aerosols of Specific Haptens by Pretreatment with Aerosols of Pyribenzamine and Isuprel. Preliminary Report**
O. SWINEFORD, F. B. WESTERVELT, and L. N. TULL. *Journal of Allergy* [*J. Allergy*] **26**, 153–156, March, 1955. 2 refs.

The authors, at the University of Virginia School of Medicine, Charlottesville, have studied bronchial desensitization with aerosols of specific haptens in guinea-pigs passively sensitized by intraperitoneal injection of 0·25 ml. Type-VI antipneumococcal rabbit serum. They were challenged with an aerosol of Type-VI pneumococcal polysaccharide in a concentration of 1 to 3 mg. per ml., the degree of dyspnoea resulting being estimated arbitrarily. On the following day the animals were exposed to an aerosol of 2% tripelennamine ("pyribenzamine") or 0·5% isoprenaline ("isuprel") for 10 to 15 minutes, and immediately following this exposure they were challenged again with the specific antigen. One day later the animals were challenged with the specific antigen for a third time. While the control exposures with the antigen challenge resulted in dyspnoea, most animals were completely protected from this by the preceding inhalation of tripelennamine or isoprenaline. *H. Herxheimer*

1288. **Studies in Bacterial Allergy. VII. Bronchial Desensitization and Resensitization in Passively Sensitized Guinea Pigs**
O. SWINEFORD, L. N. TULL, and F. B. WESTERVELT. *Journal of Allergy* [*J. Allergy*] **26**, 157–169, March, 1955. 8 refs.

The investigation reported in this paper carries further the authors' studies in bacterial allergy at the University of Virginia Medical School, Charlottesville. In the experiments now described, designed to study the problem of local resensitization following desensitization, guinea-pigs which had been passively desensitized by intraperitoneal injection of Type-VI and Type-VIII antipneumococcal rabbit serum were challenged with aerosol of 0·01 to 0·5% solution of pneumococcal polysaccharides of the same two types. It was found that when the animals were exposed repeatedly to these aerosols they became desensitized. From this it was concluded that multiple sensitization and desensitization could be achieved by this method; and, further, that desensitization of the bronchi could also be effected if the challenging doses were given intraperitoneally and were small enough to avoid a fatal result. When pneumococcal polysaccharides were used as sensitizing agent and the rabbit antiserum as challenging aerosol no anaphylactic symptoms were observed, although these were present if the antiserum was given by injection. In a number of animals which had been desensitized by repeated exposures to the antigens spontaneous resensitization occurred after an interval of 2 to 7 days. This spontaneous resensitization of passively sensitized animals after desensitization is a similar phenomenon to that observed after active sensitization. The authors are of the opinion that this problem of resensitization needs further study. *H. Herxheimer*

1289. **Further Contributions to the Vascular Physiology of Atopic Dermatitis**
R. G. WEBER, G. M. ROTH, and R. R. KIERLAND. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 19–30, Jan., 1955. 6 figs., 8 refs.

The physiological aberrations of the autonomic nervous system which have been observed in patients with atopic dermatitis were further investigated at the Mayo Clinic. In patients with atopic dermatitis or with other manifestations of atopy—for example, asthma, hay-fever, or urticaria—but without dermatitis and in healthy controls a cold pressor test was performed, the basal metabolic rate was estimated, and skin temperature was measured under standard conditions in heated rooms. Skin temperature was also measured after the subject had taken a standard quantity of alcohol.

The results, which are expressed in graphs, confirmed a previous finding—namely, that peripheral vasoconstriction occurs in patients with atopic dermatitis on exposure to a cold room and then to a hot room. Observation of temperatures in the antecubital and popliteal fossae, however, revealed less vasoconstriction in the cold and more rapid vasodilatation in the warm environment.

Exposure to the cold room was not a prerequisite for the abnormal temperature recorded in the hot room; and relatively smaller temperature differentials evoked similar abnormal peripheral vascular responses in patients with atopic dermatitis. The findings in other cases of atopy were similar and correlated with the recognized clinical association of these disease entities. No abnormality was observed in the response to alcohol. *Benjamin Schwartz*

1290. **Pressor Drugs. IV. The Safety of Inhalational Therapy in Human Patients**
V. A. DIGILO and J. C. MUNCH. *Annals of Allergy* [*Ann. Allergy*] **13**, 257–264, May–June, 1955. 28 refs.

In view of the widespread use of symphathomimetic drugs, particularly in the form of aerosols for inhalation, the authors have investigated, at the Women's Medicine College, Philadelphia, the effects of such substances on 86 patients with hypertension, rheumatic heart disease, or coronary arterial disease and on 16 diabetics, all of whom were given inhalations of an ample amount of a 1 to 2·25% adrenaline aerosol. It was found that the pulse rate, blood pressure, blood sugar level, and electrocardiogram remained unaffected. The harmless character of adrenaline inhalation in such patients is stressed. *H. Herxheimer*

Nutrition and Metabolism

1291. **Studies on the Mode of Action of Citrate Therapy in Rickets**
E. R. YENDT and J. E. HOWARD. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **96**, 101–115, March, 1955. 12 refs.

In 1939 Shohl and Butler reported (*New Engl. J. Med.*, 1939, **220**, 515) the curative effect of citrates on infantile rickets. In the present study, carried out at Johns Hopkins University, Baltimore, in an attempt to elucidate this action of citrates, cartilage slices were obtained from the tibia of rachitic rats which had been fed for brief periods on a diet containing a mixture of citric acid and sodium citrate.

Although no sign of healing in the cartilage could be detected microscopically, it was found in studies *in vitro* that the cartilage from the citrate-treated animals, when incubated in various solutions, calcified in those containing significantly lower amounts of calcium and phosphate than was required for cartilage from untreated control animals. Other rachitic rats were then given intraperitoneal injections of sodium acid and disodium phosphates (citrate having proved too toxic) and it was found that cartilage from these animals (although without histological evidence of healing) also calcified in solutions of lower calcium and phosphate concentration than was necessary for those from controls. In further studies it was shown that a significant rise in the serum phosphate concentration soon followed the addition of a citrate mixture to the diet of rats made rachitic by being fed on a high-calcium, low-phosphorus diet.

The authors suggest that the administration of citrate cures rickets by raising the serum phosphate level, and that once the process of calcification has begun, further crystals of calcium and phosphate continue to be deposited even in the presence of serum concentrations of calcium and phosphate which would otherwise be too low to initiate the process. *B. Nordin*

1292. **Mineral and Protein Metabolism and Adrenocortical Function in Senile Osteopathies.** (Le métabolisme minéral-protidémique et la fonction corticosurrénale dans les ostéopathies séniles)
M. MORPURGO, G. MARS, C. BONESSA, and A. BOSELLI. *Presse médicale* [*Presse méd.*] **63**, 312, March 2, 1955. 11 refs.

The study here reported from the Institute of Medical Hydrology, Milan, was undertaken in order to clarify the relationship between osteoporosis and osteomalacia (a subject of much controversy) and to evaluate the role of the adrenal cortex in the metabolism of protein in these osteopathies. It was carried out on 19 cases of senile osteoporosis and 10 cases of osteomalacia, 9 subjects who showed no radiological evidence of decalcification serving as controls. Nearly all the 38 subjects were women, ranging in age from 54 to 93 years, who had been admitted to hospital suffering from chronic disease; all patients in whom there was clinical evidence of hepatic or renal insufficiency were excluded from the study.

Estimation of the serum concentrations of calcium, phosphorus, alkaline phosphatase, total protein, albumin, alpha, beta, gamma, and total globulin, and measurement of the urinary excretion of calcium, 17-ketosteroids, and 11-corticosteroids all gave results which fell within the normal range. The conclusion is therefore drawn that " too sharp a distinction . . . has been made between osteoporosis and osteomalacia ".

[This investigation failed to achieve its aims. No balance studies were performed and no details of intake or excretion of the various metabolites are given. The method employed can give only very limited information, which is insufficient to justify the authors' conclusion.] *P. D. Bedford*

1293. **The Action of Phenylbutazone on the Uric Acid Content of the Plasma and Erythrocytes in Relation to Clinical Phenomena.** (Action de la phénylbutazone sur l'acide urique plasmatique et globulaire. Relations avec les phénomènes cliniques)
M. LÉVY and R. M. SICHÈRE. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 225–233, March, 1955. 6 refs.

There are apparently several hundred methods of determining the uric acid level in the blood, but none is entirely satisfactory. In this paper from the Hôpital Rothschild, Paris, the authors describe their own method which, if not more accurate than the others, at least has the merit of simplicity. In this the uric acid is determined by a modification of the method of Folin and Denis, first on the plasma, and then on heparinized whole blood, the object of heparinization being to prevent retraction of the erythrocytes. From these two results together with the haematocrit value the uric acid content of the erythrocyte can readily be calculated.

Using this method the authors showed that the uric acid level in the erythrocytes in a group of patients during attacks of acute gout was " remarkably high ", but was not always accompanied by a rise in the plasma uric acid level. The reduction in uric acid level following administration of phenylbutazone to these patients was much more marked in the erythrocytes than in the plasma; also, in the course of the treatment the pain of acute gout often subsided simultaneously with the fall of the uric acid level in the erythrocytes.

In a group of non-gouty subjects also it was found that a high level of uric acid in the erythrocytes was often accompanied by a normal level in the plasma; some of these patients had some other form of arthralgia, while others had some metabolic disorder or migraine.
Joseph Parness

Gastroenterology

1294. **Familial Incidence of Ulcerative Colitis and Ileitis**
J. FELSEN and W. WOLARSKY. *Gastroenterology* [*Gastroenterology*] **28**, 412–417, March, 1955. 19 refs.

A review of the literature reveals that the familial incidence of ulcerative colitis and regional ileitis varies from 1·3 to 11·3%. The authors cite, among others, a number of cases of regional ileitis in close relatives and of ulcerative colitis in twins. They then report a series of 38 cases (seen at the Bronx Hospital, New York, out of a total of 1,204 cases of chronic ulcerative colitis and ileitis) which occurred in 21 family groups, all possible close family relationships being observed. A number of case histories are described, including 2 instances of ulcerative colitis in husband and wife. Several patients had previously suffered from bacillary dysentery. The authors suggest that the secondary cases in their series were due to contact infection.

[The authors, in previous work, favoured the view that there is an association between bacillary dysentery and ulcerative colitis; in the present paper certain evidence, though tenuous and capable of other interpretations, is advanced in support of this view.] *J. Naish*

OESOPHAGUS

1295. **Spontaneous Perforation of the Esophagus; Experimental Study**
E. L. BRACKNEY, G. S. CAMPBELL, A. P. THAL, and O. H. WANGENSTEEN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **88**, 307–310, Feb., 1955. 1 fig., 8 refs.

Spontaneous linear perforation of the lower third of the oesophagus occasionally occurs, and various theories have been advanced to account for this, the most usual being that there is an increase of intraluminal pressure to bursting point, as may occur in severe vomiting. In this paper is described a series of experiments carried out at the University of Minnesota, Minneapolis, in which dogs were caused to vomit by obstructing the pylorus with a thread ligature. In order that peptic secretion should be maximal, each dog received 30 mg. of histamine in beeswax intramuscularly each day. To maintain hydration and electrolytic balance, intravenous fluids were administered. Of the 20 dogs in this experiment, 2 developed oesophageal perforation in a few hours; a further 10 were found to have severe oesophagitis at post-mortem examination. In 7 dogs subjected to gastrectomy in addition to the above procedure, the oesophagus being anastomosed to the pyloric antrum, no perforation or oesophagitis occurred. Of 25 dogs subjected to cervical oesophagostomy in addition to pyloric ligation, 10 died of oesophageal perforation and another 9 were found to have oesophagitis. When gastrectomy was added to the last-mentioned procedures in 4 dogs no perforation or oesophagitis occurred.

The authors conclude that oesophagitis due to peptic regurgitation lowers the bursting pressure of the dog's oesophagus (which is very high) to levels which are found in the oesophagus during vomiting. The perforation is a linear tear, usually in the upper third of the oesophagus. The results after oesophagostomy demonstrate the protective action of salivary mucus.

[In the abstracter's opinion the knowledge acquired by these experiments does not justify the severe suffering which must have been inflicted on these animals.]
A. G. Parks

See also Pathology, Abstract 1179.

STOMACH AND DUODENUM

1296. **Experimental Observations on the Etiology of Gastric Carcinoma. I. A Theoretical Analysis of the Problem. II. The Effect of Heat, Browned Overheated Fats, Food Dyes and Carcinogenic Hydrocarbons on the Gastric Mucosa**
A. C. IVY. *Gastroenterology* [*Gastroenterology*] **28**, 325–344 and 345–359, March, 1955. 2 figs., bibliography.

In the first of these two papers from the University of Illinois, Chicago, a theoretical analysis of the problem of the aetiology of gastric carcinoma is presented. A survey of the hypothesis of cancer causation leads the author to the conclusion that these tumours may be predetermined by the genes or arise as a result of an inherited susceptibility plus the action of agents which irritate, specifically or non-specifically, the cells of the gastric mucosa. However, the fact that environmental factors are known to influence their development excludes the hypothesis that this is solely determined by the genes. Both chronic gastritis and gastric ulcer due to chronic irritation or abnormality contribute to the genesis of gastric carcinomata. Though gastric polyps may become malignant, they occur too infrequently to account for most gastric carcinomata, and this also applies to congenital heterotopia.

Data showing the influence of external environment on the incidence of gastric cancer and the dependence of mortality rates on such factors as race and nationality, sex, social class, and location of ulcers and cancers are given in tabular form. A table is also included to show that, although the mortality from gastric cancer has definitely decreased in the United States since 1933, the number of deaths from all causes and from cancer of the colon and rectum has increased.

The general inference drawn is that malignant change is induced in genetically susceptible cells of the gastric mucosa either by (1) non-specific irritants acting on the marginal cells of a gastric ulcer or causing the changes seen in chronic gastritis, or (2) the action of a specific gastric carcinogen in the margin of an ulcer or on the normal gastric mucosa.

In the second paper are summarized the results of 12 years of experimental work on non-specific and specific carcinogenic factors involved in the induction of gastric carcinoma. The effects of hot drinks and food, browned, overheated fats, food-colouring dyes, feeding of carcinogenic hydrocarbons in the presence and absence of gastric ulcer, and the embedding of methylcholanthrene in the submucosa of the glandular stomach are described.

The studies showed that mucous secretion and shedding of superficial mucous cells protect the gastric epithelium from water-insoluble carcinogens, but that the presence of chronic gastritis or gastric ulcer permits them to gain contact with stem mucous cells in the crypts of the glands. Water-soluble carcinogens may be directly absorbed and incite malignant change. Overheated fat (350° C.) when fed at medium dietary level (14%) to rats for several months produced gastritis but no malignant tumours, but proved to be a low-grade carcinogen when injected subcutaneously. In further experiments 27 certified food dyes were fed to rats at 4% concentration. Five of the dyes produced gastritis and 7 lymphomata over a period of 6 to 20 months, 3 dyes caused cirrhosis of the liver and a hepatoma, and 2 of them induced fibrosarcomata when injected subcutaneously. The implantation of threads impregnated with methylcholanthrene into the submucosa of the stomach in rats caused malignant tumours to develop in some cases, but no gastric tumours were produced by feeding this carcinogen to rabbits whether chronic gastric ulcer was present or not at the time of the experiment.

The ingestion of over-hot food and drinks is suspected to cause injury to the stomach and thus may be involved in the genesis of gastric carcinoma. In the development of cancer, whether due to non-specific irritants or carcinogens, the sequence of morphological changes is similar—that is, injury, non-specific hyperplasia of mucous cells, hyperplasia (adenomatous in type), and invasion. *H. G. Crabtree*

1297. **Vagotomy with Gastroenterostomy for Duodenal Ulcer**

M. J. Bennett-Jones and S. O'Domhnaill. *British Medical Journal* [*Brit. med. J.*] **1**, 1183–1185, May 14, 1955. 12 refs.

Of some 240 of the authors' patients subjected since 1948 to vagotomy combined with a low gastro-jejunostomy for duodenal ulcer at St. Helen's Hospital, Liverpool, 95 were operated on between 4 and 6 years ago. All of these have now been traced and 90 of the 95 examined, 5 having died in the interval; in only one of these, however, could the cause of death be associated with the operation. Of the others, 79 have had no symptoms suggestive of recurrent ulceration, and most have no symptoms at all. In 4 cases there were slight attacks of pain, probably due to recurrent ulceration, and in 7 in which ulceration definitely recurred a second operation was performed. In 2 of these an insulin test meal showed that vagotomy was incomplete. In those with recurrent ulcers the symptoms seemed to suggest that these were predominantly in the duodenum, although at the second operation the duodenum was always found to be healed. More recently 10 more patients have also undergone secondary operations, at which one gastric and 2 stomal ulcers were encountered; in one of the former cases the vagotomy was incomplete. There was no mortality from the secondary operations. A Billroth-I conversion was found the most satisfactory operation for relief of symptoms in the failures, " which are not all due to recurrent ulceration ".

Summing up, the authors consider that 88% of patients operated on 4 to 6 years ago have had very satisfactory results from vagotomy and gastro-enterostomy, and that further, most of the failures have been relieved by secondary operations.

[The results in this series suggest that there is an encouraging alternative to primary partial gastrectomy in the treatment of duodenal ulcer.] *C. J. Longland*

1298. **Gastroenterostomy and Vagotomy in the Treatment of Duodenal Ulcer**

V. A. Weinstein, L. J. Druckerman, A. S. Lyons, and R. Colp. *Annals of Surgery* [*Ann. Surg.*] **141**, 482–487, April, 1955. 15 refs.

The authors have, during 7 years at Mount Sinai Hospital, New York, performed gastro-enterostomy with or without vagotomy in 101 cases of duodenal ulcer. Apart from 12 cases in which the combined procedure was carried out for purposes of evaluation, gastro-enterostomy alone or with vagotomy was selected on the grounds that gastrectomy was contraindicated. Altogether gastro-enterostomy was performed alone in 28 cases and combined with vagotomy in 73. There were 5 deaths in the series—a mortality of 5%, as compared with a mortality of less than 1% for gastrectomy in better-risk cases. The recurrence rate is given as 10% in the series in which gastro-enterostomy with vagotomy was performed, and as 15% in the small series treated with gastro-enterostomy alone. [The figures for recurrences are of little value, as some of the cases in both series were observed for only one year after operation. Therefore the abstracter is of the opinion that the various conclusions drawn from these figures are without solid foundation.]

Norman C. Tanner

1299. **The Treatment of Duodenal Ulcer by Vagotomy and Gastro-jejunostomy**

R. L. Holt and A. F. Robinson. *British Journal of Surgery* [*Brit. J. Surg.*] **42**, 494–502, March, 1955. 6 figs., 8 refs.

The authors report their results following the combined procedures of vagotomy and gastro-jejunostomy in an unselected series of 243 patients with chronic duodenal ulceration operated on between 8 and 2 years previously at the Manchester Royal Infirmary. There was only one death in the series, which resulted from severe diarrhoea. The commonest postoperative complications were of pulmonary origin.

After operation nearly half the cases (113) became achlorhydric and almost as many (102) hypochlorhydric; in 27 (11%) the acid level rose sufficiently after the

injection of insulin to suggest that the vagotomy had been incomplete.

A careful follow-up was carried out in the cases, numbering 124, operated on more than 3 years previously, the authors noting that less than 3 years is not long enough for conclusions to be drawn. Of these 124 patients, 6 became lost to follow-up and 8 died of causes unrelated to the operation and to the original disease. According to Visick's grading, results in the remaining 110 cases were satisfactory in 87% (96) and unsatisfactory in 13% (14). Among the poor results there were no proven stomal ulcers, but 2 patients had ulcer symptoms and 2 others a haematemesis. Vomiting was the commonest cause of dissatisfaction. Other, though infrequent, causes of discomfort were mild dumping, loss of energy, diarrhoea, and the need to restrict the diet. Body weight was increased after operation in nearly 60% of the cases and reduced in about 15%.

The authors' over-all impression of the operation is very favourable. *Norman C. Tanner*

1300. **Role of Duodenum in the Control of Gastric Secretion**

E. L. Brackney, A. P. Thal, and O. H. Wangensteen. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. exp. Biol. (N.Y.)*] **88**, 302–306, Feb., 1955. 2 figs., 12 refs.

Sokolov in 1904 showed that peptic secretion was inhibited when fat or weak hydrochloric acid was instilled into the duodenum. In this paper from the University of Minnesota, Minneapolis, the authors describe an attempt to amplify Sokolov's observations. Isolated gastric pouches of the Heidenhain type were created in 8 dogs and the secretion from them was measured during fasting and in response to a meat meal. A second operation was performed on 5 of the animals which consisted in removing the entire duodenum (except the proximal 2 cm.) with about 20 cm. of jejunum. Biliary and pancreatic ducts were reimplanted into the proximal jejunum, which was anastomosed to the duodenal remnant attached to the pylorus. In the remaining 3 dogs the duodenum (excepting the proximal 2 cm.), together with the first part of the jejunum, was transplanted into the mid-portion of the small gut. The biliary and pancreatic ducts continued to discharge into the transplanted loop. Alimentary continuity was re-established by anastomosing the proximal jejunum to the pylorus.

In both groups of animals there was a great increase in gastric secretion from the pouch, varying from 84 to 820% but averaging about 150%. The authors consider that removal of the duodenum from its normal position causes an increase in gastric secretion by removing a normal hormonal inhibitory mechanism which depends on the passage of gastric juice over the duodenal mucosa. They suggest that this is a factor in the production of anastomotic ulcers in man following gastrectomy and in dogs following the Mann–Williamson operation.

A. G. Parks

See also Pathology, Abstracts 1193–4.

LIVER

1301. **The Cerebral and Peripheral Uptake of Ammonia in Liver Disease with an Hypothesis for the Mechanism of Hepatic Coma**

S. P. Bessman and A. N. Bessman. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 622–628, April, 1955. 1 fig., 23 refs.

In this paper from the Research Foundation of the Children's Hospital, Washington, D.C., the authors report an investigation of the ammonia levels in peripheral arterial and venous blood and cerebral venous blood of patients with and without liver disease. In patients without liver disease the ammonia level of the peripheral blood was normal; no significant difference was observed between peripheral arterial and jugular venous blood values. In 13 patients with liver disease, some of whom were in hepatic coma, there was an increase in the blood ammonia level, with a positive cerebral arterio-venous difference—that is, the cerebral venous level was always lower than the peripheral arterial level. Increase in the arterial–cerebral-venous difference was proportional to the ammonia concentration of the arterial blood, to which the degree of coma could be roughly related.

The authors conclude from these findings of arterial–venous differences in ammonia content that brain and muscle convert free ammonia to a bound form that is not detectable by the method employed. Since the "utilization" of free ammonia by the brain cannot be explained by glutamine synthesis alone, it is postulated that increased glutamate synthesis occurs in hepatic coma, with a consequent disturbance of the Krebs cycle due to deprivation of α-ketoglutarate. Arterial blood ammonia values are considered to be more reliable than venous blood values. The authors suggest that ammonia intoxication may be important in conditions other than liver disease.

[This paper is a valuable contribution to the complex and controversial subject of the relationship between hepatic coma and ammonia intoxication of the central nervous system.] *W. H. J. Summerskill*

1302. **Glutamic Acid in Hepatic Coma**

J. M. Walshe. *Lancet* [*Lancet*] **1**, 1235–1239, June 18, 1955. 1 fig., 39 refs.

The results obtained with sodium glutamate in the treatment of hepatic coma are reported from University College Hospital, London. The drug was given by mouth or intravenously to 5 patients with chronic liver disease who had had one or more episodes of coma and to 2 patients with massive hepatic cirrhosis. There was some improvement in the mental state of the 5 patients with chronic liver disease, but 3 died shortly afterwards, one from massive gastro-intestinal haemorrhage and 2 from progressive hepatic failure. There was no response to treatment in the 2 patients with massive hepatic necrosis. The author discusses the amino-acid and keto-acid content of the blood and cerebrospinal fluid in patients with liver disease.

P. C. Reynell

Cardiovascular System

1303. **Pulmonary Blood Flow and Venous Return during Spontaneous Respiration**
G. A. Brecher and C. A. Hubay. *Circulation Research* [*Circulat. Res.*] **3**, 210–214, March, 1955. 2 figs., 9 refs.

In experiments on anaesthetized dogs carried out at the Western Reserve University and University Hospitals, Cleveland, blood flow was measured simultaneously in the main pulmonary artery and the superior vena cava with two 5734 vacuum-tube bristle flowmeters, the cross-sectional area of the vein and artery being kept fixed. Pressures in the superior vena cava, the pulmonary artery, and the aorta were recorded as well as the intrathoracic and endotracheal pressures.

It was found that blood flow through the superior vena cava, which was taken as representative of venous return, increased with inspiration as did the blood flow in the pulmonary artery, but that the increase in venous return occurred at least one heart-beat before augmentation of pulmonary flow. It was concluded that augmentation of venous return during inspiration was responsible for the increase in pulmonary flow, which occurred despite an increase in resistance in the pulmonary bed during inspiration. Variations in the blood flow in the superior vena cava during the phases of respiration were greater than those in the pulmonary artery, suggesting that some of the rapidly inflowing blood is stored in the right heart during inspiration and that this larger residual volume is then released during the expiratory phase.

G. M. Little

See also Pathology, Abstract 1210.

1304. **Idiopathic Recurrent Pericarditis. Comparison with Postcommissurotomy Syndrome; Considerations of Etiology and Treatment**
W. Dressler. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 591–601, April, 1955. 1 fig., bibliography.

The clinical and laboratory findings in 12 cases of idiopathic pericarditis were compared with those in 24 cases of the post-commissurotomy syndrome. There was a striking similarity between the findings in these two conditions, pericarditis, pleurisy, and pneumonitis being common to both. Prominent features in both were pain of the pleuropericardial type and fever. The author states that the clinical course in cases of idiopathic pericarditis and the post-commissurotomy syndrome is almost invariably benign but that relapses are frequent. Since the post-commissurotomy syndrome is believed to be a manifestation of rheumatic activity he suggests that at least some cases of idiopathic pericarditis are of rheumatic aetiology. In support of this view he draws attention to the relatively high incidence of other major and minor rheumatic manifestations in his own and in reported cases of idiopathic pericarditis and to the beneficial and often dramatic response to salicylates in this condition.

James W. Brown

1305. **Pulmonary Arterial Pressures in Persistent Ductus Arteriosus with Particular Reference to Older Patients**
R. J. Shephard. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **104**, 46–50, 1955. 1 fig., 1 ref.

At Guy's Hospital, London, pressure in the pulmonary artery was studied by cardiac catheterization in a number of patients with a left-to-right shunt. The frequency and degree of increased pressure in the pulmonary artery appeared to be less in patients with patent ductus arteriosus than in those with atrial or ventricular septal defects. Since the average size of the shunt was similar in the three groups, the differences would appear to be determined by pulmonary vascular resistance, which is less in the patient with patent ductus arteriosus. An analysis of the findings in 32 patients with the latter condition indicated that there was a tendency for the pulmonary resistance to increase with age.

J. A. Cosh

DIAGNOSTIC METHODS

1306. **Certain Clinical States and Pathologic Changes Associated with Deeply Inverted T Waves in the Precordial Electrocardiogram**
R. D. Pruitt, C. H. Klakeg, and L. E. Chapin. *Circulation* [*Circulation (N.Y.)*] **11**, 517–530, April, 1955. 8 figs., 8 refs.

Commenting that the T wave in the electrocardiogram (ECG) often shows a disturbing but intriguing refusal to conform to expected behaviour, the authors report, from the Mayo Clinic, an attempt to correlate the clinical and ECG findings in 110 cases which were selected for study because the ECG showed deep inversion of the T wave in any or all of the precordial leads 1 to 6. The cases were divided into five groups: (1) in 62 cases T in V3 was inverted at least 5 mm. and was at least as deep as T in V5; (2) 20 cases showed in addition relatively minor changes in the QRS complex; (3) in 13 cases R in V5 and V6 was tall and of the type seen in left ventricular hypertrophy; (4) in 6 cases there were changes suggestive of right ventricular hypertrophy or of partial or complete right bundle-branch block; (5) in 9 cases T in V3 was inverted less than 5 mm.

Analysis of the clinical findings showed that of cases in Group 3 there had been clinical manifestations of cardiac infarction in 25% and symptoms of severe coronary insufficiency in 65%, whereas in Group 4 no patient had shown such symptoms. Of the cases in Group 1, 69% presented substantial evidence of coronary arterial disease; of 25 patients in this group studied for at least 6 months, only 4 (suffering from constrictive pericarditis, aortic stenosis, polyneuritis, and hypertension respectively) failed to show reversion of the T wave to an upright position, and of the other 21 cases, 20 showed clinical evidence of myocardial infarction or of severe coronary insufficiency. In Groups 3 and 5

approximately half of the patients suffered from angina pectoris. A post-mortem study in 9 cases showed healed subendocardial infarction in the anterior or lateral wall of the left ventricle in 8.

Theoretical considerations, borne out by the cardiographic records of one very fully documented case, lead the authors to suggest that, while deeply inverted T waves in a direct or semidirect lead do not necessarily imply preponderant epicardial ischaemia, such inversions are probably associated with transmurally disposed regions of ischaemia, under which there may lie a subendocardial zone of myocardial infarction. *R. S. Stevens*

CHRONIC VALVULAR DISEASE

1307. **The Surgical Treatment of Aortic Insufficiency**
C. P. Bailey and W. Likoff. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 388–416, Feb., 1955. 24 figs., 11 refs.

The authors conclude from their experience that aortic insufficiency is a disease whose course is much less benign than has commonly been supposed. Rheumatism and syphilis are the most frequent causes of the valvular lesion, arteriosclerotic deformities being less common. Regurgitation may occur through a rigid, stenotic opening resulting from fusion of the commissures, or it may be the result of weakening of the aortic annulus, while both factors may be present in the same patient.

The symptoms consist in fatigue, shortness of breath, syncope, and anginal attacks and are associated with a forceful heart-beat and marked pulsation of the arteries.

None of the various methods tried for the surgical treatment of aortic insufficiency has yet proved entirely satisfactory. Hufnagel's apparatus, consisting of a plastic tube containing a non-return ball-valve, can be inserted into the aorta and prevents regurgitation beyond that point, but it cannot be placed sufficiently near to the aortic annulus to abolish reflux entirely. In the authors' experience pericardial pedicles and flaps placed across the aorta just above the valve tend to shrink and fibrose and do nothing to reduce the size of the annulus.

The authors have experimented with prostheses of various types and materials, the most successful of these "polliwogs" being a ball of nylon mesh suspended in the aorta just above the valve by two "tails" fixed to the vessel wall. Such devices are suitable for cases of aortic regurgitation with coexistent stenosis, commissurotomy being performed before insertion of the ball. Otherwise when valve cusps are normal and regurgitation is due to dilatation of the annulus the treatment adopted by the authors has consisted in trying to remedy the functional insufficiency by narrowing or constricting the annulus by means of a nylon "sash" or band passed through the muscle of the left ventricle below the right coronary artery and, on the other side, below the left coronary artery, and through the septum between aortic and pulmonary trunks, a procedure of considerable difficulty.

The authors describe in detail the techniques of these two types of operation. The former procedure has been carried out on 7 patients with 2 operative deaths, 4 of the survivors having shown considerable clinical benefit; the latter procedure has been used in 5 cases, with 2 deaths, 2 of the survivors being improved. (In a footnote the authors report the treatment of 18 further patients by one or other of these methods, with 5 deaths. Most of the survivors are stated to have shown marked benefit.) *T. Holmes Sellors*

1308. **Rupture of the Aortic Valve. A Therapeutic Approach**
J. J. Leonard, W. P. Harvey, and C. A. Hufnagel. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 208–212, Feb. 10, 1955. 1 fig., 25 refs.

Rupture of the aortic valve—the valve sometimes being normal, but more usually congenitally abnormal or the site of rheumatism, syphilis, or atheroma—may follow trauma, strain, or bacterial infection. It leads to free aortic insufficiency, carrying a grave prognosis. The trauma is usually a sudden compression of the chest such as by a kick from a horse. Severe pain and syncope or unconsciousness may be followed by a buzzing sensation in the chest, and there is a musical diastolic murmur. Similar injuries may cause rupture of the interventricular septum, usually at the base, sometimes after an interval of several days; a harsh systolic murmur and pulmonary congestion follow. Rupture of an aortic valve may be immediately fatal or cause death within a few days; if the hole caused is small the patient may live several years, but the majority survive a few months only.

Until recently there has been no effective treatment, but the case is reported here of a patient who was at work without symptoms 14 months after an operation carried out at Georgetown University Hospital, Washington, D.C. This was a boy of 17 in whom rupture of a normal valve followed a kick in the chest from a stallion. Cardiac catheterization showed an associated interventricular septal tear. After insertion of a plastic aortic valve in the first part of the descending aorta the blood pressure, formerly 180/40 mm. Hg, returned to normal and the diastolic murmur decreased.

[No details of operative technique are given.]
M. Meredith Brown

1309. **A Clinical Evaluation of the Surgical Management of Combined Mitral and Aortic Stenosis**
W. Likoff, D. Berkowitz, C. Denton, and H. Goldberg. *American Heart Journal* [*Amer. Heart J.*] **49**, 394–406, March, 1955. 1 fig.

Commissurotomy for combined mitral and aortic stenosis has been carried out on 74 patients at Hahnemann Medical College and Hospital and the Bailey Thoracic Clinic, Philadelphia, and the results are here reviewed. In 11 patients aortic and mitral stenosis was uncomplicated by other lesions; none of these patients died. In the remainder, 20 of whom died, insufficiency of one or both of these valves or another valvular lesion was also present. Before operation all the patients complained of becoming easily tired and of dyspnoea; nearly all had been under treatment for several years. When first seen about half of them had signs and symptoms of

congestive heart failure, and in just over half atrial fibrillation was present. In all cases aortic systolic and mitral diastolic murmurs were heard. Usually the heart was enlarged and the electrocardiogram was abnormal. The relative importance of the two valve lesions could generally be assessed from physical signs and symptoms, syncope and angina indicating aortic-valve involvement and haemoptysis and oedema indicating mitral-valve involvement; the latter was three times more common than the former, giving enlargement of the left atrium and the right ventricle.

Mortality was highest among patients with accompanying aortic insufficiency, the common cause of death being embolism. Nearly half of the patients who survived operation developed heart failure or atrial fibrillation. Of 41 patients followed up for at least 3 months, 34 were improved, 3 being entirely free from symptoms. Febrile reactions were observed in 10 patients, the aetiology being obscure in 7. The murmurs usually persisted, but changes in intensity were often noted. There was a significant decrease in the size of the heart in 12 of the 35 patients with cardiac enlargement. Peripheral oedema seldom improved.

It is concluded that the " primary indication for combined commissurotomy is the presence of mitral and aortic stenosis which results in significant and progressive abnormal physiology. . . . additional lesions with the possible exception of mitral insufficiency and congestive heart failure are contraindications ".

M. Meredith Brown

1310. The Clinical Results in the First Five Hundred Patients with Mitral Stenosis Undergoing Valvuloplasty

L. B. ELLIS and D. E. HARKEN. *Circulation* [*Circulation (N.Y.)*] **11**, 637–646, April, 1955. 28 refs.

In this paper from the City and Peter Bent Brigham Hospitals and Harvard Medical School, Boston, the authors review the clinical results in their first 500 cases of valvuloplasty for mitral stenosis. To lessen the risk of the development of cerebral embolism the technique in the earliest cases included passing tapes beneath the innominate, carotid, and subclavian arteries during manipulation. It was found, however, that the procedure did not always prevent this complication and it has therefore been abandoned. Discussing the selection of patients the authors state that operation should not be performed unless the patient is substantially disabled.

For purposes of comparison of results the cases are divided into consecutive series of 100 cases. Among patients in Groups II and III (classification of the New York Heart Association) operative mortality has fallen from 14% to less than 3%. On the other hand mortality among patients in Group IV has remained about 25% throughout the series. The mortality was high in the presence of auricular fibrillation; age, however, did not appear to be a significant factor.

A total of 442 patients survived operation and were followed up for 6 months to 5 years (average 22 months). Of these, 340 (77%) were markedly or moderately improved, 37 slightly improved, 34 unchanged, and 11 were worse; there were 18 late deaths and 2 patients were lost to follow-up. Embolism developed at the time of operation in 42 patients, 32 of whom had auricular fibrillation. Since this complication was seen in only 5 patients after operation the authors consider that valvuloplasty substantially reduces the risk of embolism developing. The condition regressed after initial improvement in only 31 cases in the entire series, causative factors being aortic valvular disease and mitral incompetence, although in some instances the original operation was thought to have been inadequate.

Discussing the clinical findings after valvuloplasty the authors state that the objective improvement was by no means so dramatic as the subjective. *J. R. Belcher*

1311. The Electrocardiogram in Mitral Stenosis before and after Commissurotomy

J. GIBERT-QUERALTÓ, M. TORNER-SOLER, and I. BALAGUER-VINTRO. *American Heart Journal* [*Amer. Heart J.*] **49**, 548–561, April, 1955. 4 figs., 6 refs.

In the study here reported from the Cardiological Clinic, University of Barcelona, the electrocardiographic (ECG) findings in 16 patients with pure mitral stenosis were correlated with the haemodynamic findings obtained by means of cardiac catheterization; in 8 cases the ECG changes after commissurotomy were also investigated. Preoperatively 4 patients had auricular fibrillation, the others sinus rhythm. In 9 of the 12 patients with sinus rhythm, abnormalities of the P wave were found preoperatively (width exceeding 0·1 second, diphasic waves in V1); of 6 patients with an abnormally high P wave, 5 had pulmonary hypertension. On studying the ventricular complexes a pattern characteristic of right ventricular hypertrophy was found only in patients with pulmonary hypertension—the systolic pressure exceeding 60 mm. Hg—whereas in the cases with a normal or borderline pattern or one of right bundle-branch block pulmonary hypertension was absent or slight, though the last-mentioned variety was also encountered in patients with marked pulmonary hypertension. After commissurotomy the pattern of right ventricular hypertrophy disappeared in 2 cases and became less marked in the remaining 4. *A. Schott*

1312. Mechanical and Myocardial Factors in Rheumatic Heart Disease with Mitral Stenosis

R. M. HARVEY, M. I. FERRER, P. SAMET, R. A. BADER, M. E. BADER, A. COURNAND, and D. W. RICHARDS. *Circulation* [*Circulation (N.Y.)*] **11**, 531–551, April, 1955. 12 figs., 12 refs.

The authors argue that mitral valvotomy will not improve the condition in cases of rheumatic mitral stenosis in which myocardial insufficiency resulting from the rheumatic process rather than mechanical narrowing of the valvular orifice is the predominant cause of circulatory dysfunction. In support of this view they report the findings in 16 patients with mitral stenosis studied at Columbia University and Bellevue Hospital, New York. These patients could be divided into two distinct groups. The first group, of 8 patients, gave a history of almost constant, progressive disability; haemodynamic investigation showed moderate to severe pul-

monary hypertension and either a low or normal cardiac output, with diminished blood-flow response during leg-exercise. In these cases mechanical block at the mitral valve was the predominant cause of dysfunction; at surgery no mitral valve admitted the tip of the index finger. After the performance of valvotomy the pulmonary pressure fell to a greater or lesser extent, both at rest and during exercise, in every patient and the pulse pressure decreased.

The 8 patients in the second group gave a history of occasional complete incapacity, but with relatively asymptomatic intervals. The haemodynamic findings showed that pulmonary tension at rest was normal or but little raised (except in one case first seen in heart failure), but that during exercise two patterns of response were found in the pulmonary circulation, namely, very little increase in pulmonary arterial pressure in 2 cases and a sharp rise in 5 cases. Analysis of the total findings in this group suggested that myocardial insufficiency unrelated to mechanical obstruction was the predominant lesion in these cases. This was partially confirmed by the fact that the performance of valvotomy in 2 of them was ineffective.

The authors suggest that it would seem logical to insist on demonstration of the presence of pulmonary hypertension as a pre-requisite for the operation of mitral valvotomy. *R. S. Stevens*

1313. **The Diagnosis of Tricuspid Insufficiency. Clinical Features in 60 Cases with Associated Mitral Valve Disease**
G. SEPULVEDA and D. S. LUKAS. *Circulation* [*Circulation (N.Y.)*] **11**, 552–563, April, 1955. 10 figs., 35 refs.

Among 146 patients suffering from rheumatic mitral-valve disease, studied at the New York Hospital–Cornell Medical Center, associated tricuspid incompetence was demonstrated by cardiac catheterization in 60. The most constant findings were auricular fibrillation, enlarged liver, and increased size of the right atrium. Thus of the 60 patients, 58 had chronic auricular fibrillation, 53 had persistent hepatomegaly (although only 9 showed systolic expansion), and 50 suffered from orthopnoea. Right heart failure was observed in 41 cases and distension of the neck veins in 29, but systolic pulsation in only 7; ascites was present in 11 cases and slight dependent oedema in 22. A characteristic systolic murmur was heard in 11 cases, while 8 patients were cyanosed and only 2 icteric. A clinical diagnosis of tricuspid incompetence had been made in only 14 of the 60 cases, all of which presented at least two of the following signs: systolic pulsation of the veins and liver, ascites, and a characteristic murmur. A statistically significant number of the electrocardiograms of the whole group showed a low-amplitude QRS complex and delayed onset of intrinsicoid deflection in Lead V1; approximately half showed an rsR′ or incomplete right bundle-branch block pattern. Radiography revealed right atrial enlargement of moderate to marked degree in 50 cases.

Cardiac catheterization showed that instead of a fall in right atrial pressure during ventricular systole there was an increase, due to regurgitation of blood; this positive pressure wave persisted throughout systole and the peak had a plateau or dome contour, which was invariably increased during exercise. Pulmonary vascular resistance was significantly higher in cases of mitral-valve disease associated with tricuspid insufficiency than in those without this complication. The classic signs of tricuspid incompetence were present relatively infrequently and were elicited more commonly in patients having a mean right atrial pressure above 10 mm. Hg. The proportion of cases with organic changes in the valve and of those with a purely functional insufficiency could not be determined. The factors contributing to the production of tricuspid incompetence are discussed.

The authors conclude from their experience that although tricuspid incompetence is not a contraindication to mitral valvotomy, it does in some cases seem to militate against good results. They agree that prolonged evaluation in a large number of cases is needed to confirm this impression, but point out that such a study will be thwarted from the beginning if tricuspid insufficiency is not recognized preoperatively. *R. S. Stevens*

DISTURBANCES OF RHYTHM AND CONDUCTION

1314. **Adam–Stokes Syndrome. The Treatment of Ventricular Asystole, Ventricular Tachycardia and Ventricular Fibrillation Associated with Complete Heart Block**
S. R. ROBBIN, S. GOLDFEIN, M. J. SCHWARTZ, and S. DACK. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 577–590, April, 1955. 4 figs., 32 refs.

The Stokes–Adams syndrome may be precipitated either by ventricular asystole or by ventricular tachycardia or fibrillation, and in the present paper from Mount Sinai Hospital, New York, 4 cases are presented to illustrate these two different mechanisms. The authors state that adrenaline is the drug of choice in those cases in which the attack is due to ventricular asystole, but that it is contraindicated when the attack is caused by ventricular tachycardia or fibrillation. In the latter type of case they have found *iso*propyl noradrenaline (" isuprel ") to be the most satisfactory drug, quinidine and procainamide being ineffective and even harmful. *James W. Brown*

1315. **Chronic Auricular Flutter**
J. B. HOFFMAN and M. POMERANCE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 885–901, April, 1955. 8 figs., 34 refs.

A review of the literature revealed relatively few reports on the course and clinical problems of chronic auricular flutter; with the exception of one large series of cases described by Herrmann and Hejtmancik (*Amer. Heart J.*, 1950, **40**, 884 and 1951, **41**, 182) most of them were limited to individual cases. The authors therefore describe 7 cases of chronic auricular flutter seen in the past few years at Beth-El Hospital, Brooklyn, New York.

They suggest that one of the reasons for the paucity of reported cases is that the condition is often misdiagnosed. A slow and regular ventricular rate may

suggest a diagnosis of sinus rhythm, while a varying degree of heart block may lead to a diagnosis of auricular fibrillation. Although the electrocardiogram will, in most cases, reveal auricular flutter, 3 cases are cited in which it indicated, respectively, regular sinus rhythm, auricular fibrillation, and a supraventricular tachycardia. The authors therefore advocate the use of an "auricular lead" in which the precordial electrode is placed to the right of the sternum between the first and fourth intercostal spaces.

Discussing complications, the authors state that the incidence of thrombo-embolism in cases of chronic auricular flutter is not known, but that the danger "is not insignificant". At necropsy on one of the 3 patients in their series who died suddenly no evidence of thrombo-embolism was found. The relative merits of digitalis and quinidine in treatment are discussed; it is pointed out that in a "considerable proportion" of cases of chronic flutter regular sinus rhythm is not restored by administration of these drugs. *J. Warwick Buckler*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1316. Cardiac Glycosides in the Treatment of Cardiogenic Shock

R. GORLIN and E. D. ROBIN. *British Medical Journal* [*Brit. med. J.*] **1**, 937–939, April 16, 1955. 16 refs.

At the Peter Bent Brigham Hospital, Boston, 4 patients suffering from cardiogenic shock secondary to myocardial infarction were treated with lanatoside C or ouabain. There was a remarkable clinical response in all 4 patients, with a rise in blood pressure, decrease in pulmonary oedema, and recovery from coma; all but one survived.

It is pointed out that shock in myocardial infarction may be due either to a lowered peripheral resistance or to a diminished cardiac output following acute myocardial failure, the latter, in the authors' view, being the more important factor. They recommend that in cases of cardiogenic shock vasoconstrictor drugs should be given to increase systemic resistance and blood pressure and cardiac glycosides to increase cardiac output. The dose of digitalis used should be between one-quarter and one-half of that usually given initially to the "average cardiac patient" in order to diminish the risk of toxic complications. *Keith Ball*

1317. Operations for Coronary Artery Disease

C. S. BECK and D. S. LEIGHNINGER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1226–1233, Nov. 27, 1954. 9 figs., 18 refs.

In this important paper the authors state their present views on the surgical treatment of coronary arterial disease and summarize the experience gained at the Western Reserve University School of Medicine and University Hospitals, Cleveland, Ohio, in 4,000 to 5,000 experimental operations on dogs and 186 operations on patients with coronary disease. Their attitude towards operative treatment is based on the following premises. (1) Surgery cannot arrest the occlusive process or cure the disease in the coronary arteries, nor can it restore degenerated myocardial tissue. (2) To allow time for the development of a collateral circulation, at least 6 months should elapse after a coronary occlusion before operation is undertaken. (3) It has been established by experiment that the "trigger mechanism" whereby impulses originating in an ischaemic area of myocardium may destroy the normal mechanism of cardiac contraction and lead to death from ventricular fibrillation can be inhibited by an increase in the rate of blood flow of as little as 1 to 5 ml. per minute. Hence an operation which results in even a small increase in the flow of blood to the critical area of myocardium may protect the heart from the immediate effects of a subsequent occlusion of a major coronary artery by preventing the trigger from functioning and thus give time for the collateral circulation to be developed.

By measurement of the change in coronary blood flow resulting from different experimental procedures, two operations were devised which could be expected to improve the coronary circulation. (I) Abrasion of the pericardium, application of an irritant such as powdered asbestos, partial occlusion of the coronary sinus where it enters the right atrium, and grafting of the parietal pericardium and mediastinal fat to the surface of the heart. (II) An operation to divert arterial blood into the coronary sinus, carried out in two stages: (1) insertion of a free vein graft between the aorta and the coronary sinus (or direct anastomosis of the vessels), followed 2 or 3 weeks later by (2) partial occlusion of the coronary sinus where it enters the right atrium. This raises the pressure in the sinus and produces a retrograde flow of arterial blood. Experiments on dogs showed that Operation II reduces the mortality and the size of the infarct resulting from ligation of the descending or circumflex branch of the left coronary artery to a greater extent than I, and gives a greater backflow in these two branches. However, the operation is more difficult, must be carried out in two stages, and carries a higher mortality; moreover, in the dog the graft loses contact with the capillary bed after 2 months and there is reason to believe that the same may occur in the human heart. The authors have therefore abandoned Operation II in recent years.

Of the 186 operations on human subjects, 37 were performed between 1932 and 1942 and 149 between 1945 and 1954. The operative mortality in the 3 years 1951–3 was 2·8% for thoracotomy alone, 7·5% for Operation I, and 26·1% for Operation II. There were only 2 deaths among the 27 patients operated on in 1954.

Of 33 patients surviving 3 months to 5 years after Operation I, the pain was completely relieved or markedly reduced in 84·8% (28), and 78·6% (26) were better able to work than before operation; of 43 patients who had undergone Operation II, pain was relieved or reduced in 88·4% (38) and 79·1% (34) were capable of more work. [No details are given of the survival times after operation in the whole series.]

In the authors' opinion the most acceptable type of patient for operation is "a lean person in the 40's or 50's who has had the disease for a year or more, has

pain, but is still able to get around". There is no age limit, but it is remarked that young persons often have rapidly progressive disease and their survival may therefore be shorter than the average. Patients with cardiac failure from myocardial degeneration and those in whom the heart is dilating are regarded as unsuitable, but those with moderate enlargement and those with status anginosus are accepted.

[It is notoriously difficult to assess the results of operations for coronary disease owing to the unpredictable nature of the disease in that one patient may improve without operation, whereas in another the disease may progress.] *F. J. Sambrook Gowar*

HEART FAILURE

1318. Studies on the Continuous Use of a Carbonic Anhydrase Inhibitor (Diamox) in Ambulatory Patients
R. A. Massumi and J. M. Evans. *American Heart Journal* [*Amer. Heart J.*] **49**, 626–632, April, 1955. 1 fig., 12 refs.

The effect of "diamox" (2-acetylamino-1:3:4-thiadiazole-5-sulphonamide) in the treatment of 30 patients with oedema, due to congestive heart failure in all but 3, is described in this paper from the George Washington University School of Medicine, Washington, D.C. The dosage of the drug, which was given for periods ranging from 1¼ to 8½ months (average 4 months) to 28 of the patients, was adjusted according to the individual's response, 250 to 750 mg. being administered by mouth in one dose in the morning for periods of 3 to 5 days weekly. The results were "good to excellent" in 19 cases (63·3%), but less satisfactory in patients with long-standing and recurrent right-sided heart failure. Side-effects included paraesthesiae, giddiness, headache, nausea, and vomiting; they occurred 30 to 60 minutes after ingestion of the drug, before any demonstrable biochemical changes had taken place, and the authors suggest that they were the result of a direct action on nerve cells. Fatigue and drowsiness, on the other hand, occurred late and were often accompanied by a fall in the serum carbon dioxide combining power and potassium level, which was attributed to shifts in the sodium–potassium equilibrium. Altogether, side-effects occurred in 9 patients and were sufficiently severe in 2 of these for treatment to be discontinued. The drug is regarded as a safe and effective oral diuretic for use in ambulatory patients. *A. Schott*

1319. Acute Pulmonary Infection and Cardiac Failure in Chronic Emphysema
K. Braun and G. Izak. *American Heart Journal* [*Amer. Heart J.*] **49**, 385–393, March, 1955. 3 figs., 25 refs.

The clinical and laboratory findings in 7 cases of cor pulmonale in which congestive cardiac failure was precipitated by lung infection are reported from the Rothschild–Hadassah University Hospital, Jerusalem. All the patients had had spastic bronchitis for 4 to 8 years and were readmitted to hospital because of increased cough, fever, dyspnoea, palpitation, and peripheral oedema. The clinical, radiological, and electrocardiographic findings were typical of cor pulmonale. Venous pressure ranged from 20 to 29 cm. of water and circulation time varied from 18 to 24 seconds. In all cases there was a significant decrease in vital capacity and maximum breathing capacity, while in 6 cases there was also retention of carbon dioxide. In one patient on whom cardiac catheterization was performed the pulmonary arterial pressure before and after oxygen therapy was 135/45 mm. Hg and 93/20 mm. Hg respectively; in one other case the pulmonary arterial pressure following recovery from heart failure was 30/8 mm. Hg. Treatment consisted in a low-sodium diet and administration of antibiotics, diuretics and, in some cases, digitalis or ACTH. All the patients responded to this treatment with a decrease in signs of cardiac failure, improved ventilatory function, and reduced venous pressure.

The authors discuss the factors which may lead to raised pulmonary pressure—including bronchopneumonia causing reduction in functioning lung parenchyma, direct action of anoxia or carbon dioxide retention, and fever causing an increased metabolic rate. They point out that in some cases the clinical picture is complicated by respiratory acidosis due to carbon dioxide retention. This may be aggravated rather than relieved by oxygen therapy as the anoxic stimulus to the respiratory centre is removed; in such cases artificial respiration is indicated. *D. Goldman*

1320. Transcapillary Migration of Heavy Water and Thiocyanate Ion in the Pulmonary Circulation of Normal Subjects and Patients with Congestive Heart Failure
L. S. Lilienfield, E. D. Freis, E. A. Partenope, and H. J. Morowitz. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 1–8, Jan., 1955. 3 figs., 14 refs.

In order to study the rates of transfer of water and ions across the pulmonary capillary bed the authors, working at Georgetown University Medical Center, Washington, D.C., injected into the basilic vein, or in 4 cases directly into the pulmonary artery through a cardiac catheter, a mixture of the non-diffusible substance azovan ("Evans") blue and the diffusible materials deuterium oxide (heavy water; D_2O) and thiocyanate ion.

Serial samples drawn from the femoral artery at 2-second intervals during the succeeding 60 seconds showed that at first the concentration of deuterium oxide and of thiocyanate was more reduced (mean loss 42%) than that of azovan blue, indicating a loss of heavy water and thiocyanate from the pulmonary circulation. Towards the end of the 60 seconds, however, the concentrations of heavy water and thiocyanate in the blood samples rose to a level higher than the calculated expected concentrations, and were less reduced than that of azovan blue.

In 7 normal subjects quantitative estimation of the maximum volume of D_2O which was present outside the pulmonary capillaries (the extravascular water space of the lung) indicated that this space had a mean volume of 190 ml., while in 7 patients with congestive cardiac failure the mean volume was 290 ml. This is a relatively

small extravascular space compared with that of the forearm as previously reported by the authors (*J. appl. Physiol.*, 1953, **5**, 526). The authors conclude that the size of the pulmonary extravascular space is proportional to the pulmonary blood flow in normal subjects but not in patients with cardiac failure. The capillaries of the lung appeared to be relatively impermeable to thiocyanate as compared with those of the forearm; only small amounts left the pulmonary circulation in normal patients, and the amount was only slightly more in patients with cardiac failure. *T. B. Begg*

1321. **The Cardiohemodynamic Effects of Venous Congestion of the Legs or of Phlebotomy in Patients with and without Congestive Heart Failure**
W. E. JUDSON, W. HOLLANDER, J. D. HATCHER, M. H. HALPERIN, and I. H. FRIEDMAN. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 614–621, April, 1955. 1 fig., 8 refs.

In studies carried out at Massachusetts Memorial Hospitals, Boston, it was shown that on acute reduction of the "effective blood volume" by removal by venesection of up to 720 ml. of blood or by producing congestion of the legs by means of cuffs, normal subjects and patients with heart disease but no symptoms of heart failure responded by a significant fall in cardiac output. When the same procedure was carried out on patients with congestive heart failure most of them showed a rise in cardiac output. Of the latter, one had tricuspid incompetence and the performance of venesection apparently reduced the reflux into the left atrium. Patients with cor pulmonale showed a response to venesection similar to that of normal subjects.

The authors point out that while these results are in rough conformity with previous work, they were unable to correlate the changes in cardiac output with a fall in the filling pressure of the heart, and thus their findings neither confirm nor refute any interpretation based on Starling's law. *J. McMichael*

1322. **Oral Mercurial Diuretics: Mercumatilin in the Treatment of Congestive Heart Failure**
S. P. DIMITROFF, R. C. LEWIS, M. C. THORNER, and J. B. FIELD. *American Heart Journal* [*Amer. Heart J.*] **49**, 407–413, March, 1955. 5 refs.

Mercumatilin, a new diuretic, was tried in the treatment of 25 patients, mainly out-patients, at Los Angeles County Hospital, Los Angeles, California, who had previously received other mercurial diuretics. It was given by mouth in tablet form, each tablet containing the equivalent of 20 mg. of mercury and 20 mg. of theophylline. Most of the patients had cardiac failure resulting from hypertension or arteriosclerosis—that is, from conditions which are usually progressive. Criteria of a satisfactory response were: a reduction in the need for mercury injections, maintenance of basal body weight, minimal peripheral and pulmonary oedema, minimal increase in the size of the liver, and absence of toxic side-effects.

In 22 of the patients there was a good response, with maintenance or loss of weight without evidence of salt depletion, less dyspnoea, and often increased exercise tolerance; in a few instances an increase in the daily salt intake was possible. Most of the patients required three tablets a day, two or three times a week, or about one tablet daily. Of the 3 patients who failed to improve, one had undergone mitral commissurotomy, one had coronary arterial disease, while one with hypertension improved initially, but took an excessive amount of salt. One patient required parenteral as well as oral administration of mercury but in reduced dosage. Except for nausea and diarrhoea in one patient who had suffered from gastritis, there was no evidence of intolerance or toxicity, albuminuria, or change in blood chemistry over several months, although most patients were between 50 and 70 years of age. The authors emphasize that oral administration of a diuretic means less discomfort for the patient and fewer domiciliary or hospital visits. *D. Goldman*

BLOOD VESSELS

1323. **Coarctation of the Aorta with Special Reference to the First Year of Life**
W. T. MUSTARD, R. D. ROME, J. D. KEITH, and A. SIREK. *Annals of Surgery* [*Ann. Surg.*] **141**, 429–436, April, 1955. 3 figs., 9 refs.

The incidence of and mortality from the infant (preductal) and adult (postductal) forms of coarctation of the aorta are discussed and the findings in 90 cases seen at the Hospital for Sick Children, Toronto, during a recent 10-year period are reviewed. It is stated that the incidence of coarctation of the aorta is about 1 in 10,000, that two-thirds of the patients have signs or symptoms in infancy, and that only one-third of the children with this abnormality at birth survive the first year of life, 60% of those with postductal and 89% of those with preductal coarctation dying from heart failure.

Discussing the diagnosis, the authors state that coarctation should be suspected in an infant when dyspnoea and a heart murmur are present and the femoral arterial pulse is not palpable; in some patients with the preductal form of coarctation, however, no heart murmur is elicited. Unless the patient is in marked heart failure the blood pressure is higher in the arms than in the legs. The electrocardiogram may indicate enlargement of the left or the right ventricle, but is often not helpful. In patients with cyanosis, which usually indicates the presence of some severe associated defect, the coarctation can be demonstrated by venous angiography; in other cases an aortogram is more helpful and permits differentiation between the two types of constriction.

Early operation is indicated in most cases, especially if heart failure is marked or does not respond to digitalis and the heart is enlarged, but a concomitant respiratory infection precipitating failure must first be controlled. At operation wide exposure and sufficient mobilization of the aorta and ductus must be obtained; this is facilitated by the great elasticity of the vessels. In the baby the left common carotid artery can safely be clamped and this may be necessary if the hypoplastic area includes that artery; in these circumstances the aorta should be

divided very obliquely, a longitudinal cut being added if necessary to obtain approximation and good anastomosis after removal of the affected segment of the aorta. It is not known whether the anastomotic suture line will grow with the child. The use of stored grafts is not recommended.

Surgical excision was carried out on 5 infants with the postductal type of coarctation without a death. Of 10 infants with the preductal type subjected to operation, 5 died, usually from severe associated defects. All the survivors, including an infant aged 11 days, improved; blood pressure returned to normal with relief of heart failure. *M. Meredith Brown*

1324. **The Use of Hexamethonium in Treatment of Arteriosclerosis Obliterans**

J. H. WINDESHEIM, G. M. ROTH, and R. W. GIFFORD. *Circulation* [*Circulation (N.Y.)*] **11**, 604–608, April, 1955. 5 figs., 7 refs.

Hexamethonium ion in increasing doses of 10 to 50 mg. was given subcutaneously to a group of 11 patients with severe arteriosclerosis of the lower extremities. Three additional patients were given 10 mg. but not the larger doses because of the hypotensive effects of the drug. Two patients responded to the drug with a slight to moderate increase in skin temperature of the toes. Two others showed slight vasodilatation in the less ischemic lower extremity, but none in the limb with more severe arteriosclerosis obliterans. The skin temperature of the toes in the remaining 10 patients did not change after the injections of hexamethonium.

From this study it is concluded that hexamethonium is not effective in the treatment of severe arteriosclerosis obliterans. Since the blood pressure decreased after injection of the drug, we assume that vasodilatation occurred in blood vessels unaffected by the arteriosclerotic process.—[Authors' summary.]

1325. **Further Experience with Long-term Anticoagulant Therapy**

W. T. FOLEY, E. MCDEVITT, C. SYMONS, and I. S. WRIGHT. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 497–502, April, 1955. 12 refs.

Anticoagulant drugs were given for an average of 3½ years (range 1 to 8 years) to 85 out-patients suffering from various diseases characterized by thrombo-embolic episodes at the New York Hospital–Cornell Medical Center, and in this paper the results are reviewed. The patients visited the hospital once a week, when the prothrombin time was estimated and the daily dose of the anticoagulant drug for the following week determined; in some instances fortnightly visits only were necessary. A prothrombin time of 20 to 35 seconds (normal 13 to 16 seconds) was regarded as safe for long-term therapy. Dicoumarol was given to 73 patients, ethyl biscoumacetate to 10, "cycloumarol" to one, and phenindione to one. The dosage remained fairly constant for any given patient, but upper respiratory infection, diarrhoea, administration of antibiotics, and a low food intake caused variations.

Of one group of 25 patients with rheumatic heart disease who had had more than one attack of thromboembolism (totalling 113 such attacks in 765 patient-months), 7 had 18 attacks over a period of 1,128 patient-months of anticoagulant therapy; the remaining 18 in the group had no further attacks. Four others with rheumatic fever who had had a single attack of thromboembolism experienced no further attack during 218 patient-months of treatment. Of 24 patients suffering from recurrent thrombophlebitis (92 thromboembolic episodes over a period of 2,207 patient-months), 7 had one attack each during 896 patient-months of treatment; there were no other complications in this group. In a group of 11 patients who had had myocardial infarction more than once (49 episodes in 587 patient-months without anticoagulant therapy) there were only 3 episodes during 393 patient-months of treatment, while in a group of 12 who had had one attack of myocardial infarction there was one questionable episode in 554 patient-months. Similar satisfactory results were obtained in a miscellaneous group of 9 patients.

Haemorrhage, usually mild, occurred in 31 cases during treatment; in 7 of them in which haemorrhage occurred when the prothrombin time was within the therapeutic range there was some associated condition to account for it. Of the 18 deaths in the series, 17 were related in the main to the primary disease, not to anticoagulant therapy; one patient died from cerebral haemorrhage while under treatment elsewhere. In a few cases in which prothrombin time was unduly prolonged (50 to 90 seconds) 10 mg. of vitamin K_1 was given orally or intramuscularly; this had some effect within 3 to 4 hours, the full effect being observed at 12 hours.

J. N. Agate

HYPERTENSION

1326. **Parenteral Reserpine in Treatment of Hypertensive Emergencies**

W. M. HUGHES, J. H. MOYER, and W. C. DAESCHNER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 563–577, April, 1955. 6 figs., 9 refs.

In this paper from the Jefferson Davis Hospital (Baylor University College of Medicine), Houston, Texas, the parenteral administration of reserpine is shown to be effective where urgent, but not immediate, reduction of blood pressure is desired. The results of such treatment in three groups of patients with hypertension are reported: (1) 14 patients with severe hypertensive cardiovascular disease, mostly with Grade-IV retinopathy; (2) 6 patients with pre-eclampsia; and (3) 8 children with acute glomerulonephritis.

With doses of 2·5 to 10 mg. (given either intravenously diluted in 100 ml. of 5% dextrose solution or intramuscularly without dilution) in adults and of 50 to 100 μg. per kg. body weight in children a sustained decrease of blood pressure was obtained in all cases except one of those in Group 3, normal levels being attained in 9 of the 14 cases in Group 1, all of those in Group 2, and 6 of the 8 in Group 3. The maximum effect occurred 2 to 5 hours after injection and was

maintained for periods varying from 2 to 24 hours. The slow nature of the response allowed it to be controlled easily, and excessive hypotension was rare. Side-effects, apart from sedation, were prominent only if the dose or frequency of administration was unduly increased; they included weakness and conjunctival injection in most cases, while after several days' treatment muscle tremors were noted in some cases, developing in one into a Parkinsonian syndrome. All these stopped on withdrawal of the drug.

The dosage of reserpine varied from 2·5 to 5 mg. at intervals of 4 to 12 hours in Group 1, and from 2·5 to 10 mg. at intervals of 8 to 24 hours in Group 2. In Group 3 a dose of 25 to 100 μg. per kg. was given and repeated when the blood pressure had returned to hypertensive levels, it rarely being necessary to give more than one dose a day. Parenteral treatment was continued for 3 to 17 days in Group 1, 1 to 7 days in Group 2, and 1 to 4 days in Group 3, being then replaced by oral treatment with reserpine or other hypotensive drugs.

[There seems little doubt about the value of parenteral reserpine in suitable cases, but the control periods allowed in this study were inadequate for a full appraisal of its effects to be made as compared with those of other factors, notably bed rest.] *P. Hugh-Jones*

1327. **Effects of Parenterally Administered Reserpine**
E. L. Rea and J. F. Fazekas. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 538–539, April, 1955. 1 fig., 5 refs.

The administration of large doses (4 to 15 mg.) of reserpine parenterally in order to achieve a rapid quietening effect on acutely agitated patients is reported from the District of Columbia General Hospital, Washington, D.C. The results obtained in 9 cases, mostly of alcoholism, show that the drug is often ineffective for this purpose and may be dangerous. Skin flushing [presumed to be due to the drug], orthostatic hypotension, and shock developed in 3 patients; one died in spite of treatment with intravenous noradrenaline, and an electrocardiogram taken just before death is interpreted as showing a direct toxic action of reserpine on the myocardium.

[The use of parenteral reserpine for this purpose (which the authors have now abandoned) would seem to be unwarranted in view of these results and of the existence of other safe and effective drugs.] *P. Hugh-Jones*

1328. **Radical Sympathectomy in Arterial Hypertension. I. Immediate Results in 122 Cases.** (Les sympathectomies étendues dans l'hypertension artérielle. I. Résultats immédiats à propos de 122 interventions)
R. H. Martin and M. Bonamy. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **48**, 240–244, March, 1955.

The authors briefly recount the steps, dating from 1935, by which they have developed a technique of radical sympathectomy for the treatment of hypertension based on that of Poppen. In the present form of the operation 10 to 12 sympathetic ganglia are removed together with all the splanchnic nerves; removal of one adrenal gland or of its medulla is being added.

At the Hôpital Gouïn, Clichy, 122 patients have undergone sympathectomy of varying extent since 1947, with 12 postoperative deaths; some of those patients who died would not now be regarded as suitable candidates for the operation. The postoperative complications included intractable intercostal pain, pleural effusion, cerebral disturbances, and transient anuria. Orthostatic hypotension appeared in 2 cases only and was transitory. The authors consider that operation should be avoided in patients over 40 years of age if the mortality is to be kept low and troublesome complications avoided. *C. J. Longland*

1329. **Radical Sympathectomy in Arterial Hypertension. II. Long-term Results.** (Les sympathectomies étendues dans l'hypertension artérielle. II. Résultats éloignés)
F. Joly, A. Mathivat, J. R. Sicot, L. Gerbaux, and M. Touche. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **48**, 245–276, March, 1955. 2 figs., 17 refs.

This paper deals in considerable detail and from a variety of aspects with a series of 80 patients treated at the Hôpital Lariboisière and the Hôpital Boucicault, Paris, by radical sympathectomy for arterial hypertension. [In an abstract it is possible only to pick out a few points of interest. In general the findings are similar to those reported in other series, but the reader who is specially interested in the subject will find much interesting material in the original paper.]

Almost all the patients treated had essential hypertension; in 23 cases the disease progressed to a fatal outcome after operation, leaving 57 survivors who were examined after 2 to 6 years. In nearly every case the blood pressure before operation was above 210/120 mm. Hg, and in more than half the optic fundi showed changes of Grade III or IV. In approximately one-third of the patients surviving for over 2 years the blood pressure returned to normal and there was a lasting general amelioration of symptoms. In another third, despite improvement in the fundi and in the cardiac state, the blood pressure eventually returned to the pre-operative level. In the remainder little benefit was obtained. Striking regression of fundus changes was a frequent finding. The occurrence of cerebrovascular accidents could not be related causally to operation. In half of the 44 cases in which serial electrocardiograms were taken the abnormalities seen before operation disappeared, though in a few cases the improvement was only transitory. In a similar proportion of cases an enlarged heart became smaller, usually within a month. Renal function was improved in only 3 of the 20 patients studied, while in 10 cases it had deteriorated 4 years or more after operation. Renal biopsy was performed on most of the patients and the findings are described and discussed; in more than half of the most severe cases no " malignant " arteriosclerotic lesions were found.

The presence of malignant hypertension is considered by the authors to be a contraindication to operation, which, it is suggested, should be reserved for young patients with severe hypertension but without gross visceral damage. *C. J. Longland*

Haematology

ANAEMIA

1330. **Erythrocyte Destruction in Sickle-cell Anemia: Simultaneous N^{15}-Hemin and N^{15}-Stercobilin Studies**
G. W. James and L. D. Abbott. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **88**, 398–402, March, 1955. 2 figs., 22 refs.

This paper from the Medical College of Virginia, Richmond, describes an attempt to study erythrocyte destruction and haemoglobin turnover in a severe case of sickle-cell anaemia with ^{15}N-glycine, used in small amounts so as to minimize the period of labelling of newly-formed erythrocytes and the re-utilization and peripheral incorporation of the isotope. The concentration of ^{15}N was determined after its administration in the circulating haemin and also in faecal stercobilin. The patient, a 21-year-old negro male with 100% of haemoglobin S, was in a stabilized haematological state with a haemoglobin concentration of 6 g. per 100 ml. blood and a reticulocyte count of 23%. He was given 1·0 g. of 31 atom % excess ^{15}N-glycine by mouth in two equal doses at an interval of 4 hours. A normal male of about the same weight as the patient was used as a control.

Estimations of the rate of disappearance of ^{15}N from haemin and stercobilin indicated a close correlation between the rate of erythrocyte destruction and the excretion of the isotope in faecal stercobilin. The apparently exponential disappearance of the isotope from haemin was consistent with indiscriminate, random destruction of erythrocytes in sickle-cell anaemia. The rate of turnover of haemoglobin in this case was 6·3% per day, corresponding to a mean erythrocyte survival time of about 16 days. There was no evidence of more than one population of erythrocytes.

It is pointed out that in view of the wide variations in the severity of the disease in different cases of sickle-cell anaemia, it is probable that factors as yet unknown may be involved in the haemolytic process in this condition. *A. J. Duggan*

1331. **Blood Changes Resulting from Intravenous Iron Therapy. Storage of Hemosiderin in Lymphocytes and Monocytes.** [In English]
B. J. Koszewski. *Acta haematologica* [*Acta haemat. (Basel)*] **13**, 217–225, April, 1955. 1 fig., bibliography.

In view of the possible dangers of overloading with iron by administration of some of the new saccharated iron oxide preparations recently made available the author has investigated, at the University of Zürich Medical School, the changes in the blood following the intravenous injection of saccharated iron oxide in 18 patients, of whom 16 suffered from anaemias of various types and 2 were not anaemic but had inoperable cancers. The solution used contained 20 mg. of iron per ml. and a daily dose of 100 mg. of iron was administered for varying periods of time, the total dose ranging from 0·5 g. in 24 days to 4·3 g. in 55 days. The 2 non-anaemic patients received respectively 1·3 g. in 15 days and 3·0 g. in 35 days. The blood was examined frequently, the films being stained by the May–Grünwald–Giemsa technique and all likely iron-containing cells marked. The films were stained for iron by removing the Giemsa stain by immersion in a mixture of saturated ammonium sulphide and 70% alcohol for 1 to 3 hours, and then placing them for one hour in absolute alcohol containing a few drops of saturated ammonium sulphide. After washing with double distilled water they were treated with 20% ferricyanide and 1% HCl for 10 minutes, washed, and counter-stained with safranin.

In most cases there was an increase in the erythrocyte count, but in no case was there a significant change in the total or differential leucocyte count. There were striking changes in leucocyte morphology, however, haemosiderin inclusions being noted in 16 cases. Iron was present mainly in the lymphocytes—in up to 25% of these cells in some cases—and less frequently in the monocytes. In a few cases reticulum cells containing iron granules appeared in the circulation. Iron inclusions were not found in the neutrophil, eosinophil, or basophil granulocytes. In cases in which the anaemia was not due to loss of iron from the body the inclusions appeared after 0·4 to 0·7 g. of iron had been given over 5 to 9 days. In cases of anaemia associated with chronic haemorrhage, 1·1 to 1·4 g. over 14 days was required to produce iron inclusions. In the 2 non-anaemic patients, who died of carcinomatosis, there was marked haemosiderosis in the liver and spleen; these 2 patients had received about 2 g. iron in about 3 weeks.

The author considers that the presence of iron inclusions indicates phagocytic activity by the lymphocytes, which occurs when iron is accumulated in the system. He recommends that intravenous iron therapy should be stopped immediately lymphocytic inclusions appear. *M. Lubran*

1332. **Iron-deficiency Anaemia in Pregnancy**
P. B. B. Gatenby and E. W. Lillie. *Lancet* [*Lancet*] **1**, 740–743, April 9, 1955. 2 figs., 18 refs.

An investigation of the occurrence of iron-deficiency anaemia in pregnancy was carried out on 4,314 women attending the antenatal clinic of the Rotunda Hospital, Dublin, during the course of one year. It was found that in 1,027 (24%) of these women the haemoglobin level was below 10 g. and in 389 (9%) below 9 g. per 100 ml. at their first visit, a low haemoglobin value being more prevalent during the winter months. A group of 397 of these patients, most of them with a haemoglobin level of 7 to 9 g. per 100 ml., were studied in a special clinic. Among the symptoms looked for—dyspnoea,

tiredness, anoxia, epistaxis, and headache—dyspnoea was by far the most common, occurring in 182 cases (45%), with tiredness (88, or 22%) next, and it is suggested that too little attention is paid to these symptoms in pregnancy. About one-third of the 397 patients (136) had no symptoms indicative of anaemia.

The possible predisposing factors were examined. Half of the patients seldom or never ate meat, and about one-quarter of them had had menorrhagia, or anaemia in a previous pregnancy. There appeared to be some relationship between the frequency of anaemia and parity, but this was not very marked.

Treatment was with ferrous sulphate and ferrous gluconate. Intolerance to the drug was noted in 97 (48%) of the 207 patients receiving ferrous sulphate, in 38 (41%) of 91 given " molybdenized " ferrous sulphate, and in 9 (8%) of 109 given ferrous gluconate. Apart from the degree of intolerance there did not appear to be any difference in the responses to the sulphate and gluconate. The authors conclude that to counteract iron deficiency an effective preparation of iron should be administered to every pregnant woman during the last trimester.

R. F. Jennison

1333. **Water Diuresis in Pernicious Anaemia**

W. H. TAYLOR. *Clinical Science* [*Clin. Sci.*] **13**, 497–509, Nov., 1954. 2 figs., 17 refs.

It is known that the diuresis which follows the ingestion of water is sometimes delayed in pernicious anaemia. In an attempt to elucidate some of the factors responsible the author, at the Radcliffe Infirmary, Oxford, carried out water-diuresis tests on 25 healthy subjects and 45 patients with pernicious anaemia.

The total volume of urine excreted in 2 hours after the patient had drunk one litre of water—which was the measure of water diuresis—was markedly less in patients with untreated pernicious anaemia than in treated patients, and in both groups was significantly less than in healthy subjects. The maximum excretion of urine in healthy subjects occurred 60 to 90 minutes after ingestion of water and usually exceeded 10 ml. a minute; in pernicious anaemia the maximum excretion was delayed and diminished, especially in untreated cases. No significant correlation was observed between the 2-hourly volume of urine excreted and the haemoglobin level, the age of the patient, or the duration of the anaemia.

Since delayed diuresis in anaemia may be due to delay in absorption from the gut or in renal excretion, an attempt was made to determine the role of each factor by estimating the concentration of plasma chloride and of total blood solids before and after treatment. In 3 out of 5 patients with untreated pernicious anaemia there was a fall in plasma chloride concentration, the maximum being reached much later than in controls; there was also a more prolonged interval between this point and the peak of the diuresis compared with the controls. In 4 of the 5 patients a concentration, not a dilution, of blood solids was observed 20 minutes after drinking water, and maximum dilution was delayed. After treatment of the anaemia for 6 or 7 days the diuretic response improved, becoming normal in 2 of the 5 patients, while the pattern of dilution of plasma chloride and total blood solids became normal in 4.

It is suggested that in pernicious anaemia there are delayed water absorption and delayed renal excretion, and that treatment with vitamin B_{12}, liver extract, or folic acid restores water absorption to normal but that the delay in renal excretion may persist.

Nigel Compston

1334. **The Binding of Vitamin B_{12} by Castle's Intrinsic Factor**

L. RAINE. *Nature* [*Nature* (*Lond.*)] **175**, 777–778, April 30, 1955. 5 refs.

Although the degree of binding of vitamin B_{12} (cyanocobalamin) by protein complexes with intrinsic-factor activity is not necessarily correlated with the degree of that activity, it may be related to its absorption into the human body. It has been shown by the author in experiments carried out at the Royal Victoria Infirmary, Newcastle upon Tyne, that the amount of vitamin B_{12} bound by a preparation of intrinsic factor to which it is added in excess is dependent chiefly on the concentration of the vitamin, but that binding is also increased, though to a lesser extent, by an increase in the concentration of intrinsic factor. In some experiments ultrafiltration was used to separate the free vitamin B_{12} from the complex before assay with an *Escherichia coli* mutant, and in others the free vitamin was assayed in the presence of the complex. The results obtained by the two methods were comparable.

These results are of interest in view of clinical observations that the haematopoietic effect of vitamin B_{12} and intrinsic factor given together by mouth may be enhanced by raising the dosage of either. It is possible that the consequent increase in binding, as demonstrated *in vitro*, may result in increased absorption of the vitamin *in vivo*.

J. Naish

1335. **Oral Treatment of Megaloblastic Anaemia with Small Amounts of Vitamin B_{12} and Intrinsic Factor.** [In English]

P. BASTRUP-MADSEN and L. PAULSEN. *Acta haematologica* [*Acta haemat.* (*Basel*)] **13**, 193–206, April, 1955. 6 figs., 21 refs.

At the County Hospital, Aarhus, Denmark, daily doses of 15 μg. of vitamin B_{12} together with 0·15 g. of desiccated hog pyloric mucosa were given orally to 13 patients, 9 of whom had true Addisonian anaemia, and double these doses was given to 6 patients, of whom 4 had Addisonian anaemia. Of the remaining patients, 5 had megaloblastic anaemia secondary to disturbances of the gastro-intestinal system, and in one additional case of Addisonian anaemia treatment had to be discontinued because of an allergic response to the hog mucosa.

The reticulocyte response was satisfactory in 16 cases; it was absent in 3 cases, of which 2 were cases of non-Addisonian anaemia and the third was in an 84-year-old woman with Addisonian anaemia, arteriosclerosis, and an atrophic marrow who failed to respond subsequently

to all therapeutic measures. The response in the remaining non-Addisonian cases was suboptimal. There was little difference between the groups receiving different doses of vitamin B_{12}. An increase in the erythrocyte count occurred within the first 4 weeks in 16 cases, reaching a somewhat higher value (about 4,000,000 per c.mm.) in 4 of the cases treated with the higher doses. No increase occurred in the 3 cases showing no reticulocyte response. Ten patients with Addisonian anaemia were observed for several months, the erythrocyte count reaching 4,000,000 per c.mm. in 4 cases within 8 weeks, within 3 months in one, and in 7 months in one; these 6 patients had all received the smaller dose of vitamin B_{12}. In the other 4 patients, who all received the larger dose, the erythrocyte count reached 4,000,000 per c.mm. within 8 weeks. Leucopenia and thrombocytopenia, when present, were corrected within 5 weeks. A prothrombin level lower than 40% was found in 3 out of 8 cases of Addisonian anaemia studied, but the level became normal within 7 weeks of treatment.

Changes in the bone marrow were investigated in the 4 cases of Addisonian anaemia given the higher dose of vitamin B_{12}. Erythropoiesis returned to normal and granulopoiesis almost to normal in 2 weeks. In one case studied 6 hours after a single dose of 30 μg. of vitamin B_{12} and 0·3 g. of pyloric mucosa the megaloblasts had decreased in number to 50% of their initial value, and had disappeared in 5 days. The effect of the treatment on glossitis, gastro-intestinal disturbances, and mild neurological manifestations, when present, was satisfactory. In general, all the cases of Addisonian anaemia responded well to the larger dose of vitamin and mucosa, although a few responded only suboptimally to the smaller dose, whereas the 5 cases of secondary megaloblastic anaemia responded poorly or not at all to either dose. *M. Lubran*

1336. **The Vitamin-B_{12} Content and Binding Capacity of the Gastric Juice in Pernicious Anaemia and Other Diseases.** (Vitamin B_{12}-Gehalt und Vitamin B_{12}-Bindungsvermögen im Magensaft bei perniciöser Anämie und anderen Erkrankungen)
I. PENDL and W. FRANZ. *Acta haematologica* [*Acta haemat. (Basel)*] **13**, 207–216, April, 1955. 3 figs., 20 refs.

At the Institute of Physiology, University of Frankfurt, the vitamin-B_{12} content and the vitamin-B_{12}-binding power of the gastric juice were assayed microbiologically in 18 patients suffering from pernicious anaemia and in 23 controls, 8 of whom were healthy subjects and 15 were patients suffering from other gastric disturbances. In both groups the vitamin-B_{12} content ranged between 0·06 and 3·0 mμg. per ml., there being no significant difference between the control group and the pernicious anaemia group or between treated and untreated cases of pernicious anaemia.

The vitamin-B_{12}-binding power of the gastric juice, determined *in vitro*, ranged in the controls from 0·4 to 1·1 mμg. of vitamin B_{12} per ml. in 18 cases and from 0·1 to 0·25 mμg. per ml. in 5 cases. Of the 18 cases of pernicious anaemia, the gastric juice showed no binding power in 9 cases, a trace in 3, and in 6 ranged from 0·4 to 0·8 mμg. per ml. of gastric juice—that is, within the normal range.

The vitamin-B_{12}-binding power was also tested by paper electrophoresis of the gastric juice. The latter was evaporated to dryness at room temperature and dissolved in one-tenth volume of M/15 phosphate buffer at *p*H 6·5. Electrophoresis was carried out for 6 hours on a volume of 0·06 ml. Half the paper was stained for protein, the other half being cut into 1-cm. strips which were eluted with 5 ml. of water, the vitamin-B_{12}-binding power of the eluate being then determined. In general, gastric juice from the patients with pernicious anaemia contained more protein than that from the controls, but in no case could binding of vitamin B_{12} be demonstrated by paper electrophoresis in which it had been absent on testing *in vitro*. *M. Lubran*

HAEMORRHAGIC DISEASES

1337. **Congenital Hypoprothrombinemic States**
A. J. QUICK, A. V. PISCIOTTA, and C. V. HUSSEY. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 2–14, Jan., 1955. 5 figs., 39 refs.

The second stage of blood coagulation was studied in patients with congenital hypoprothrombinaemic states, the prothrombin time, the total prothrombin time, and the prothrombin consumption time being estimated by Quick's methods. Four distinct types are described: (1) panhypoprothrombinaemia, in which there is an inadequate capacity to produce prothrombin; (2) hypoprothrombinaemia due to a deficiency of free prothrombin; (3) deficiency of the stable factor (Factor VII or proconvertin); and (4) deficiency of the labile factor (Factor V or pro-accelerin).

Two families with a deficiency of Type 1 are described, 2 males being affected in one family and a female in the second. As both the affected members of the former were of the same generation, there was no evidence concerning a hereditary factor in the pathogenesis. An attempt is made to account for this defect by postulating the existence of an enzyme system ÆK, consisting of an apo-enzyme (Æ), a protein presumably produced by the liver, and a prosthetic group (K) supplied by vitamin K. The function of ÆK is to synthesize prothrombin, and it is considered that in panhypoprothrombinaemia there is a deficiency of the apo-enzyme Æ. Three families with a deficiency of Type 3 are described, in each of which there were affected members in several generations; the condition is therefore inherited. The authors consider the responsible gene to be recessive. Only homozygous individuals have a frank bleeding tendency, but heterozygous siblings have a slightly prolonged prothrombin time.

The view that prothrombin exists in both a free or active form and a bound or inactivated form has been developed by the senior author and his school over the past decade, and the finding of a family with a deficiency of the former—that is, of Type 2 above—supports this

view. The affected members of this family—a brother and sister and their mother—had a prolonged prothrombin time which was unaffected by large doses of vitamin K and only partially corrected by mixing the patient's plasma with an equal volume of normal plasma. It appears from this evidence that a further new clotting factor must be postulated. If the inhibitor responsible for the inactivation of prothrombin, whatever its nature, be designated as X, prothrombinogen is prothrombin X and the ratio of free to inactive prothrombin (prothrombinogen) may be regarded as being maintained in an equilibrium which is mediated through a "Y" factor thus: Prothrombin X + Y ⇌ Prothrombin + XY.

In the family described the affected members appear to be deficient in Factor Y, whereas the father and 3 sons are normal. The defect is apparently transmitted quantitatively, since the prothrombin time of both children was identical with that of the mother. Little is known about the Y factor; according to the authors it resembles Factor V in that it is not adsorbed by the alkaline earths. Types 1 and 2 may readily be distinguished, as a mixture of equal parts of normal plasma and Y-deficient plasma still has a slightly prolonged prothrombin time (since the concentration of Y factor has not been raised to the normal level), whereas a mixture of the same proportions of normal plasma and plasma of Type 1 has a normal prothrombin time, the normal concentration of the Y factor ensuring that sufficient active prothrombin is formed from the prothrombinogen furnished by the normal plasma. The prothrombin consumption time of Y-deficient plasma is normal, unlike that of plasma deficient in Factor V. In normal plasma the concentration of Factor Y is fixed, which accounts for the constancy of the prothrombin time. *John F. Wilkinson*

NEOPLASTIC DISEASES

1338. **Multiple Myelomatosis Treated with a Combination of Urethane and an Oral Nitrogen Mustard**
J. INNES and W. D. RIDER. *Blood* [*Blood*] **10**, 252–258, March, 1955. 3 figs., 7 refs.

This paper from the University of Edinburgh records the results of treatment with an oral preparation of urethane and a nitrogen mustard in 17 patients with multiple myelomatosis between May, 1951, and January, 1954. Nitrogen mustard alone has little influence on the disease, while urethane has the disadvantage of producing severe nausea, although it is reported to relieve bone pain, slow down the progress of the disease, and improve the anaemia. In 1949 Skipper demonstrated a possible synergistic action between urethane and methyl bis-(β-chloroethyl)-amine nitrogen mustard against chloroleukaemia 1394 in mice, with no increase in toxicity, and on the basis of this report the combined therapy was tried in multiple myelomatosis.

Gelatin capsules containing 25 mg. of β-naphthyl-di-(2-chloropropyl)-amine (R 151) and 0·5 g. of urethane were prepared and given in initial doses of 2 to 4 capsules daily, which were well tolerated, to 17 patients in an advanced terminal stage of the disease with haematopoietic depression, the diagnosis having been confirmed by marrow biopsy in all but one case. Six patients with vertebral involvement likely to cause paraplegia had localized radiotherapy as well. Treatment was continued, usually with a daily dosage of 2 capsules, for periods up to 22 months without evidence of undesirable bone-marrow depression and without causing nausea. Once initial improvement was obtained, treatment was continued in the out-patient department.

The relief of bone pain was the most striking effect of the treatment: 9 out of 15 bedridden patients became ambulant, and one returned to heavy work as a boilermaker. In 9 cases the haemoglobin level rose from 64% to 89% with treatment, in 3 there was no change in the anaemia, and in 5 it deteriorated. There was a general downward trend in the plasma globulin level and erythrocyte sedimentation rate in the successful cases. Radiographic evidence of recalcification of the bony lesions was found in 2 patients, treated for 18 and 22 months respectively, while in several other cases there was at least no evidence of progress of the disease. However, 11 of the 17 patients died during the 32-month period of observation.

As little effect is usually produced by either drug alone in doses of the order employed in this series of cases, the suggestion of synergistic action is supported by the authors' results. *I. G. Williams*

1339. **Myleran (GT 41) in the Treatment of Leukaemia.** [In English]
A. VIDEBÆK. *Acta medica Scandinavica* [*Acta med. scand.*] **151**, 295–306, April 16, 1955. 10 figs., 9 refs.

The author presents, from the Radium Centre and University Hospital, Copenhagen, the clinical histories of 10 patients suffering from acute or chronic leukaemia who were treated with 1:4-dimethanesulphonoxybutane (GT 41; "myleran"), first synthesized by Haddow and Timmis (*Lancet*, 1953, **1**, 207; *Abstracts of World Medicine*, 1953, **14**, 134).

Two of the patients died from cerebral haemorrhage during treatment, although not without showing considerable improvement in the haematological condition. In the others myleran produced remissions in 6 out of 7 cases of chronic myeloid leukaemia, the results being as good as those obtained with radiotherapy. The remaining case was first diagnosed as chronic myeloid leukaemia (leucocytes 300,000 per c.mm.) but after 58 days' treatment with myleran there were signs of incipient pancytopenia. The disease was then recognized as myelosclerosis, and after suitable treatment and many blood transfusions the patient recovered. Examination 15 months later showed that the blood picture was normal apart from a slight thrombocytopenia, and the spleen, which had originally been very large, was no longer palpable.

[No comment is made on this extraordinary result. It is usually held that in osteosclerosis the splenomegaly is compensatory; but in the case described its disappearance was accompanied by improvement.]
A. Piney

Respiratory System

1340. **A Comparison of the Efficacy of Tetracycline and Penicillin in the Treatment of Pneumococcal Pneumonia**
E. FREI, C. R. AUNER, T. E. VAN METRE, and C. G. ZUBROD. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 173–176, Feb. 3, 1955. 7 refs.

The efficacy of tetracycline was compared with that of penicillin in the treatment of 57 cases of pneumococcal pneumonia at the City Hospital, St. Louis, Missouri; 26 patients received tetracycline and 31 penicillin, the two groups being comparable as regards the severity of the infection. Tetracycline was given by mouth in a dosage of 4 g. daily and penicillin by intramuscular injection in a dosage of 600,000 units daily, the treatment in both groups being continued until the rectal temperature was 100° F. (37·8° C.) or lower for at least 48 hours. No difference was observed between the two groups in the therapeutic response, frequency of complications, or mortality. There were no side-effects with penicillin therapy, but in 8 of the patients given tetracycline untoward reactions were noted, including nausea, vomiting, and diarrhoea. Stool culture in 4 of these 8 cases revealed a pure or predominant growth of *Staphylococcus aureus*. *Thomas Anderson*

1341. **Effects of the Carbonic Anhydrase Inhibitor "6063" (Diamox) on Respiration and Electrolyte Metabolism of Patients with Respiratory Acidosis**
A. L. L. BELL, C. N. SMITH, and E. ANDREAE. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 536–546, April, 1955. 2 figs., 19 refs.

At St. Luke's Hospital, New York, the authors investigated the effects of acetazoleamide ("diamox") on electrolyte metabolism and pulmonary ventilation in patients suffering from respiratory acidosis. The administration of a single oral dose of 25 mg. of the drug per kg. body weight to 5 patients was followed by increased urinary excretion of CO_2 and a fall in the plasma bicarbonate content. This was accompanied by a rise in arterial oxygen tension (P_{O_2}) and a slight but definite rise in arterial carbon dioxide tension (P_{CO_2}), but there was no significant change in minute ventilation, or in oxygen consumption or excretion of CO_2 by the lungs. The authors suggest that the rise in arterial P_{CO_2}, accompanying a rise in P_{O_2}, is probably due to interference by acetazoleamide with the carbonic anhydrase activity of the erythrocytes, but they consider that this mechanism probably operates only when large doses of the drug are given.

When 7 patients with chronic emphysema were treated with 10 mg. of acetazoleamide per kg. body weight daily for periods of 18 to 54 days there resulted increased renal excretion of water, CO_2, sodium, and potassium, reduced excretion of chloride, and a rise in urinary *p*H. These changes did not persist after the third day of therapy despite continued administration of the drug. The plasma bicarbonate level and plasma *p*H fell initially and then rose after the third day of treatment, but never reached control levels so long as treatment was continued. In these patients the arterial P_{O_2} rose and P_{CO_2} fell, and while no consistent change in total pulmonary ventilation was demonstrated, the authors feel that the blood changes were most likely due to a prolonged slight increase in alveolar ventilation. Clinically, the patients in this latter group experienced some slight relief from their dyspnoea during the first 3 weeks of acetazoleamide therapy, but this did not endure. The patients who received a single large dose of the drug noticed no change in symptoms. Lastly, 2 patients severely ill with respiratory acidosis showed no significant improvement in the blood abnormalities in response to acetazoleamide, the fatal course of the illness being apparently uninfluenced by the drug. *Bernard Isaacs*

1342. **The Use of Acetazoleamide in Acute Respiratory Acidosis**
M. WISHART and B. ISAACS. *Lancet* [*Lancet*] **1**, 995–996, May 14, 1955. 9 refs.

Acetazoleamide, a carbonic anhydrase inhibitor, was given to 3 patients at the Stobhill General Hospital, Glasgow, who were suffering from acute exacerbation of cor pulmonale due to infection, in the hope that this drug's capacity to increase the urinary excretion of sodium, potassium, and bicarbonate, thereby lowering the serum bicarbonate level and the *p*H of the blood, might be beneficial. Despite the fact that the expected biochemical changes occurred, however, the first patient failed to improve, the second showed an immediate deterioration and died, and the third deteriorated so much after the first dose that treatment was stopped; the patient subsequently recovered. The authors suggest that the fall in serum bicarbonate level was not accompanied by a fall in carbon dioxide tension, presumably because of pulmonary insufficiency, so that there was a dangerous fall in the *p*H of the blood.
J. Robertson Sinton

1343. **Age Differences in Ventilatory and Gas Exchange Responses to Graded Exercise in Males**
A. H. NORRIS, N. W. SHOCK, and M. J. YIENGST. *Journal of Gerontology* [*J. Geront.*] **10**, 145–155, April, 1955. 3 figs., 23 refs.

The study described in this paper was undertaken to determine the reasons for the reduced physical efficiency of the ageing male, the authors selecting for this purpose three small groups of patients and staff from the Baltimore City Hospitals whose ages were respectively 25 to 29, 58 to 70, and 74 to 85. The subjects were required to do varying amounts of work at varying rates while recumbent under a bicycle ergometer, which in this case

was worked by the arms. The basal metabolic rate, pulmonary ventilation, carbon dioxide elimination, and oxygen uptake were determined before, during, and after the test. The detailed results are given in tables.

The relative inefficiency of the aged was demonstrated in increased ventilation without a proportionate increase in oxygen usage. This inefficiency was most marked when the work was performed at the higher rates, at which coordination of movement was less accurate in the elderly than in the young. The authors consider that neurological deterioration is a major factor in this loss of physical efficiency.

[The conclusions are based on the findings in a total of only 19 subjects, 5, 6, and 8 in each group respectively.]

J. Robertson Sinton

1344. **Prolonged Pulmonary Eosinophilia. A Report on Three Cases**

R. D. YOUNG. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 129–133, April, 1955. 11 refs.

NEOPLASTIC DISEASES

1345. **Some Observations on the Epidemiology of Lung Cancer**

R. FOWLER. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 485–494, April 2, 1955. 7 figs., 25 refs.

The recorded mortality from cancer of the lung in Australia increased from 7 per million persons in 1908–12 to 91 per million in 1948–52. The rate of increase (6·6% per year) was practically constant throughout, but it was greater for men (7·7% per year) than for women (4·6%). The increase was not wholly due to the increasing average age of the population, since the death rate, when standardized for age, also increased steadily; part of the increase, it is thought, must have been due to a real change in the incidence of the disease, this view being supported by the different rates of increase for men and for women.

From the records of 1,000 consecutive cases of lung cancer admitted to the 6 Melbourne hospitals co-operating with the Victorian Central Cancer Registry in 1940, 1941, and 1946–53 an analysis is presented of age and sex distribution, methods of diagnosis and of presentation, delay in diagnosis, and histology. The 5-year survival rate was 50% for patients leaving hospital after resection, but only 4% for all patients who attended hospital. More patients might be cured if all persons over 60 years of age could be examined regularly by mass radiography, but reliance cannot be placed on the treatment of established disease alone as a means of control.

Tobacco consumption in Australia remained at a fairly steady level from 1915 to 1940, but subsequently there has been a sharp increase, due almost entirely to an increase in cigarette consumption. While it is thought probable that habitual heavy smoking (particularly of cigarettes) is a potent factor in the aetiology of the disease, other inhalational hazards are also under suspicion. About 60% of the Australian population lives in the large cities, but it is impossible at present to say whether atmospheric pollution can be incriminated. The classic hazard associated with the mining of uranium ores is of particular interest now that uranium fields are about to be exploited in Australia.

Richard Doll

1346. **Bronchial Carcinoma in Printing Workers**

E. ASK-UPMARK. *Diseases of the Chest* [*Dis. Chest*] **27**, 427–435, April, 1955. 2 figs., 9 refs.

The number of cases of cancer of the lung observed annually at the Royal Academic Hospital of Uppsala increased between 1931 and 1950, twice as many cases being diagnosed in the second decade as in the first. This does not prove that there has been a real increase in the incidence of the disease in Sweden, but in view of experience in other countries it is thought likely. Even if cigarette smoking is accepted as an important aetiological factor, other possible factors must also be considered. The amount of printed material, especially newspapers, available has increased greatly during the last 50 years, and as it has been shown that malignant tumours can be produced in mice by painting their necks with printer's ink this may be one such factor. Evidence is now presented to suggest that printing workers suffer a specially high incidence of carcinoma of the lung. Out of 30 male patients observed at Uppsala up to 1931, 25 were printing workers, one being a typographer aged 31. An analysis of a series of cases reported by Wiklund in 1951 shows that out of 125 cases occurring in male residents of Stockholm aged above 40 years, 8 (6·5%) were in printing workers, whereas the expected frequency is estimated at $1{\cdot}14 \pm 0{\cdot}95\%$. The significance of these figures is enhanced when it is realized that although only about one-third of Stockholm's printing workers are exposed to printing ink, all 8 of those with lung cancer appear to have been included in this group.

Richard Doll

1347. **Bronchogenic Carcinoma: Cell Type and Other Factors Relating to Prognosis**

J. W. KIRKLIN, J. R. MCDONALD, O. T. CLAGETT, H. J. MOERSCH, and R. P. GAGE. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **100**, 429–438, April, 1955. 9 figs., 12 refs.

At the Mayo Clinic 767 histologically confirmed cases of bronchogenic carcinoma were seen between 1943 and 1949 inclusive; these, with 64 cases of bronchial adenoma, 10 of alveolar-cell tumour, and 3 of unclassified tumours, made up the total of 844 cases of primary cancer of the lung seen during this period. Classification of the 767 cases of bronchogenic carcinoma according to cell type was as follows: squamous-cell, 258 cases (33·7%); columnar-cell, 97 cases (12·6%); small-cell, 121 cases (15·8%); and large-cell (undifferentiated), 291 cases (37·9%). The histological features of each type are discussed and excellent photomicrographs are reproduced.

In 369 (48%) of the 767 cases thoracotomy was performed and in 184 of these curative resection was possible —that is, in 24% of the 767 cases. The cell type of the tumour had an important bearing on prognosis: in

patients with adenocarcinoma and squamous-celled growths the prognosis was relatively good, provided resection was possible. Resectability rates were: squamous-cell tumour 34·1%, columnar-cell 25·8%, small-cell 11·6%, and large-cell 19·6%. The prognosis was poor in cases of small-celled tumours since resection was possible in only a small proportion; the survival rate after resection in these cases was exceedingly low. The 5-year survival rates (expressed as a percentage of the original number of cases in each histological group) were: squamous-cell 11·8, columnar-cell 11, large-cell 5, and small-cell 0·8. The authors consider that heroic operations may be worth while in cases of squamous- and columnar-celled growths (provided all the growth can be removed), but that they are of doubtful value in cases of small-celled carcinoma in view of the slender chance of cure.

It was not possible accurately to assess the effect on prognosis of lymph-node involvement, but an appreciable number of patients with lymph-node metastases survived more than 3 years after operation. In the authors' experience pneumonectomy is the operation of choice in cases of squamous-celled carcinoma because pre-cancerous changes are frequently present in the proximal bronchus; in cases of peripheral columnar- and large-celled growths without nodal involvement lobectomy is usually preferred. *F. J. Sambrook Gowar*

1348. **Favorable Bronchiolar Carcinoma**
R. H. OVERHOLT, W. A. MEISSNER, and J. E. DELMONICO. *Diseases of the Chest* [*Dis. Chest*] **27**, 403–413, April, 1955. 7 figs., 3 refs.

The authors describe 15 cases of operable bronchiolar carcinoma found in a review of 507 cases of proved bronchogenic carcinoma seen at the Overholt Thoracic Clinic, Boston, Massachusetts, between 1948 and 1953. The gross and microscopic pathological appearance in these 15 cases was that of a tumour variously classified under such headings as alveolar-cell carcinoma, adenomatosis, papillary adenocarcinoma, and mucinous carcinoma. The gross resemblance to tuberculosis or to metastases from mucinous tumours of the gastro-intestinal tract and ovary was often striking. These tumours are considered to be of a low order of malignancy and slow to metastasize. The cases under review probably represent relatively early stages of growth and support the belief that these tumours can be treated by resection if seen early enough, and are monocentric rather than multicentric but eventually give rise to disseminated intrapulmonary metastases.

The patients comprised 8 females and 7 males between the ages of 46 and 67. Symptoms were few and not distinctive, while 9 patients had none at all. In 13 of the cases the condition was first diagnosed on routine radiological survey, and to 8 cases the term "coin lesions" was applied early in their clinical course. In most cases the referring doctor considered the radiological shadow to be innocuous. In one case the shadow had been present for 8 years, but in spite of such long duration no gross metastases were evident at operation. Bronchoscopic findings were negative in each instance, and the exact diagnosis in every case was based upon examination of the extirpated lobe or lung.

Because it was possible to predict that the lesion was localized, 11 of the cases were treated by lobectomy. Eight of the patients are now living without evidence of disease after 2 to 4 years, and the limited resection appears to have been sufficient. One died of cerebral metastases after 7 months, and 2 developed ipsilateral metastases. In view of the fact that bronchiolar carcinoma is of such a low grade of malignancy, a longer period of follow-up would be necessary for a definitive evaluation, but it is considered that, for localized tumours promptly treated, a conservative resection will yield as good results as pneumonectomy. *D. P. McDonald*

1349. **Late Results following Pneumonectomy and Lobectomy for Bronchogenic Carcinoma.** [In English]
H. R. SØRENSEN and F. THERKELSEN. *Acta chirurgica Scandinavica* [*Acta chir. scand.*] **108**, 375–392, 1955. 40 refs.

The results of surgical treatment of cases of cancer of the lung seen at Rigshospitalet, Copenhagen, between 1942 and 1953 are analysed. The operability rate rose from 26·7% in the period 1943–9 to 38·9% in 1950–3. Altogether, between 1942 and 1953 pneumonectomy was performed in 160 cases and lobectomy in 21, with 36 operative deaths (19·9%). The operative mortality fell from about 30% in the early years to 11·3% in 1953. The authors state that mortality from bronchial fistulae and infections was considerably lower than the figures indicated (15·3%) since embolism was a more common cause of death in 1949 to 1953 than in earlier years. Although mortality in patients over 60 years of age was almost twice that in patients under 60, the authors do not consider that this rate (21%) should be regarded as a contraindication to surgical treatment.

The survival rates among 117 patients followed up for at least one year were as follows: 12 months, 69·1%; 3 years, 48·8%; and 5 years, 41·3% (19 out of 46). Of the 117 patients, 11 had undifferentiated carcinoma and all died within 2 years (average 8·6 months); 13 had adenocarcinoma and 12 of these died within 3 years and one was alive at 4 years; 90 of the remainder had squamous-celled carcinoma and 19 of these survived 5 years, a percentage survival rate for this group of 47·5 (19 out of 40). The prognosis was poor in the presence of metastases to the hilar or mediastinal lymph nodes (average survival less than one year); the authors point out, however, that the "need for performing extrapleural dissection or pericardial resection does not exclude cure". The results of lobectomy were as good as those of pneumonectomy, but the former procedure was carried out only in the most favourable cases with localized growths and, in a few instances, as a palliative measure in elderly patients. The prognosis was best in the group of patients under 60 years of age with squamous-celled carcinoma without lymph-node metastases, 73% of such patients surviving 5 years. Of 22 patients who survived 4 or more years after resection (including 5 subjected to lobectomy), the majority had no difficulty in resuming their former occupation. *F. J. Sambrook Gowar*

Otorhinolaryngology

1350. **Aspergillosis of the Ear. A Report of Twenty-nine Cases**

E. A. STUART and F. BLANK. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **72**, 334–337, March 1, 1955. 9 refs.

A study of the literature leads the authors to suggest that otomycosis aspergillina has perhaps become more common in the Montreal area than formerly, since 29 cases of the disease were admitted to the Royal Victoria Hospital, Montreal, over a recent period of 30 months. A brief clinical account is given of each of these cases, of which 19 were due to infection with *Aspergillus niger*, 6 with *A. flavus*, 2 with *A. fumigatus*, and one each with *A. nidulans* and *A. flavipes*.

In 11 cases in which there was no history of previous ear disease the authors consider that the signs and symptoms were due solely to the mycotic infection. In the other 18 cases the infection occurred in association with eczema of the auditory meatus, chronic suppurative middle-ear disease (treated with or without the local use of antibiotics), and conditions requiring the general administration of antibiotics; in this group of cases the causal relationship of the fungus to the aural symptoms was not clear. Treatment [of which no details are given] included the local application of neomycin, tincture of merthiolate, polymyxin, "cresatin", and chloramphenicol, but to none of these substances was there a consistently good response.

[It is the abstracter's opinion that the results of treatment depended more on the minutiae of the aural toilet than on the particular drug used.]

Norman W. MacKeith

1351. **Bacteremia following Tonsillectomy. Effect of Preoperative Treatment with Antibiotics in Postoperative Bacteremia and in Bacterial Content of Tonsils**

P. S. RHOADS, J. R. SIBLEY, and C. E. BILLINGS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 877–881, March 12, 1955. 1 fig., 18 refs.

An investigation was undertaken at the Wesley Memorial Hospital and Northwestern University Medical School, Chicago, to assess the effect of the preoperative administration of antibiotics, with particular reference to the transient bacteriaemia that occurs after tonsillectomy. The findings were as follows. When blood was taken immediately after tonsillectomy from 17 patients receiving 600,000 to 800,000 units of procaine penicillin intramuscularly daily for 4 to 10 days preoperatively a positive culture was obtained in only one case (5·9%). Of 26 patients receiving 600,000 to 800,000 units of penicillin on 2 occasions only—12 to 18 hours and 1 hour—before tonsillectomy, blood culture was positive in 8 (30·8%). In a smaller group of 7 patients given 900,000 to 1,200,000 units of penicillin orally for 5 to 7 days preoperatively bacteriaemia occurred in 4 (57%). A positive blood culture was found in 17 (28·3%) of the 60 tested of a control group of 68 patients not given antibiotics before tonsillectomy. Alpha-haemolytic or gamma-anhaemolytic streptococci were obtained from blood cultures 28 times, beta-haemolytic streptococci 4 times, a combination of beta-haemolytic and gamma-anhaemolytic streptococci twice, and pneumococci once. Beta-haemolytic streptococci were found in 57·4% of cultures from the excised tonsils of the 68 patients not receiving antibiotics, although only 28·96% of preoperative throat cultures were positive. Among patients receiving penicillin intramuscularly on the day before tonsillectomy and the day of operation 31·03% of cultures of the excised tonsils contained beta-haemolytic streptococci, even though these organisms were not present in preoperative throat cultures. Only once were beta-haemolytic streptococci cultured from excised tonsils of patients receiving intramuscular penicillin daily for 4 to 10 days before tonsillectomy. Most Gram-positive organisms except micrococci and *Gaffkya tetragena* were greatly reduced in number after intramuscular injections of penicillin, but Gram-negative organisms such as *Klebsiella pneumoniae*, *Aerobacter aerogenes*, and *Escherichia coli* were found in increased numbers in cultures from the throat and excised tonsils.

The authors conclude that intramuscular injection of penicillin preoperatively for several days is required to eliminate beta-haemolytic streptococci from the depths of the tonsil and to prevent bacteriaemia after tonsillectomy. They were also able to confirm the finding of other authors that cultures of throat swabs do not give a true indication of the bacterial content of the deep tonsillar tissue.

I. Ansell

1352. **Primary Localized Amyloid Tumours of the Upper Respiratory Tract.** [In English]

O. JEPSEN and K. NIELSEN. *Acta medica Scandinavica* [*Acta med. scand.*] **151**, 321–328, April 16, 1955. 4 figs., 21 refs.

The authors suggest that amyloidosis of the larynx is less rare than is generally assumed, and that this condition should be borne in mind in the presence of uncharacteristic, non-malignant, tumour-like laryngeal lesions. Usually the condition can be diagnosed only on histological examination of a biopsy specimen. They briefly describe the features of primary and secondary amyloid disease, both forms of which may be generalized or local, and discuss the incidence, symptomatology, and differential diagnosis of amyloid tumour from other tumour-like lesions of the larynx, with reference to 5 cases of primary localized amyloidosis of the larynx seen at the University Ear Clinic and the Radium Centre, Aarhus, Denmark, in which the growth involved respectively the subglottal space, the right ventricular band, the vocal cord, the ary-epiglottic fold, and the left side of the larynx from the vocal cord to the introitus.

H. D. Brown Kelly

Urogenital System

1353. **The Mechanism of Ammonia Excretion during Ammonium Chloride Acidosis**

F. C. RECTOR, D. W. SELDIN, and J. H. COPENHAVER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 20–26, Jan., 1955. 4 figs., 21 refs.

In a study, at the University of Texas, Dallas, Texas, of the mechanism of ammonia excretion rats were given a standard electrolyte-deficient diet and various supplements of ammonium chloride. The urine was examined daily for *p*H, titratable acidity, and ammonium content, and after 1 to 14 days the animals were killed and the kidneys analysed for glutaminase activity.

The level of ammonia excretion rose from the first day and renal glutaminase activity from the second. Thereafter they rose in parallel and by the 7th day had reached maximum values, which were maintained as long as ammonium chloride was administered. The level of ammonia excretion and the degree of renal glutaminase activity were also proportional to the load of ammonium chloride, but different loads did not lead to significant variations in the *p*H of the urine. Rats which were given sodium bicarbonate or acetazoleamide, and whose urine consequently was of higher *p*H, excreted less ammonia than other rats with similar renal glutaminase activity, suggesting that rate of ammonium excretion depends on urinary *p*H at any given level of enzyme activity.

The factors responsible for the activation of renal glutaminase during ammonium chloride acidosis could not be identified. There was no correlation between this activity and serum bicarbonate concentration or tissue potassium concentration, as determined by estimation of the potassium content of muscle. *T. B. Begg*

1354. **Renal Biopsy in Pyelonephritis**

G. P. KIPNIS, G. G. JACKSON, F. D. DALLENBACH, and J. A. SCHOENBERGER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 445–459, March, 1955. 26 refs.

The authors describe the results of the investigation of chronic urinary-tract infections in 20 patients selected from the wards and out-patient departments of the Research and Educational Hospitals, University of Illinois College of Medicine. One had acute pyelonephritis; the remainder had had infected urine for many months or years, usually associated with some abnormality such as nephrolithiasis (mostly treated) or tortuous, dilated, or otherwise abnormal ureters, while one patient had polycystic kidneys. Antibiotic therapy had been unsuccessful.

In addition to complete microscopical and bacteriological examination of the urine, investigation of the blood chemistry, and renal function tests, renal biopsy was attempted in every case and was successful in 13. A Turkel needle with internal diameter of 1·6 mm. was used, the patient being placed in the prone position with a sandbag under the hypogastrium. The needle was inserted below the 12th rib on the right side lateral to the margin of the sacrospinalis muscle, the kidney site having been determined previously by intravenous or retrograde pyelography. After fixation of the needle in the kidney the stylet was replaced by the cutting needle, which was inserted a further 2 cm. by rotation. The biopsy material was withdrawn by gentle suction and divided into two parts, one being placed in formalin and the other ground with sterile sand and cultured on 7% human blood agar and eosin–methylene-blue agar, and in thioglycollate broth. No serious effects of biopsy were observed, although microscopic and, rarely, gross haematuria always followed successful biopsy; one patient suffered colic from passing clots.

Correlation of the findings showed that the patients could be divided into three groups: (1) those with infected urine but normal kidney function and structure; (2) those with chronic pyuria, morphological changes in the kidney characteristic of active chronic pyelonephritis, and disturbed renal function; and (3) those with acute or intermittent bacteriuria and with renal structural abnormalities ("scarring", hydronephrosis, polycystic changes, necrosis, or nephrosclerosis), but with variable disturbance of renal function. Examination of the urine by the usual clinical methods was insufficient for the separation of patients with chronic pyelonephritis from others. However, it was concluded that ability to concentrate urine to a specific gravity of 1026 in the absence of albuminuria and with normal urea clearance was good evidence against the presence of significant renal damage. Cultures of the urine were positive in all cases, the organisms isolated including *Escherichia coli*, *Aerobacter aerogenes*, *Staphylococcus aureus*, streptococci, and *Proteus* spp. On the other hand organisms were cultured from 2 biopsy specimens only; in each case the same organism was also found in the urine passed at about the same time. It is thus possible that some of the biopsy specimens were not representative of the whole renal tissue. On the other hand, abnormal material was never obtained from patients with normal renal function, whereas abnormal tissue was found in all cases in which there was some abnormality of function. In those cases in which pyelonephritis was diagnosed the kidney showed an increase in interstitial tissue and chronic inflammatory and fibrotic reactions. In some peritubular or periglomerular hyaline casts were commonly present in the tubules, which usually showed atrophic epithelium. The histological picture of active chronic pyelonephritis was associated with functional changes, the most important of which was a decrease in effective renal plasma flow, with proportionate and equal reduction in glomerular filtration rate and tubular mass. The reduction in plasma flow could be related to the concomitant production of hypertension. The findings in the first group of patients indicate, however, that lower urinary-tract infection, pyelitis, or even focal pyelonephritis can persist over long periods without causing measurable kidney damage. *B. G. Maegraith*

Endocrinology

PITUITARY GLAND

1355. **Hypophysectomy in Man.** (Hipofisectomia en el hombre)
R. LUFT and H. OLIVECRONA. *Folia clinica internacional* [*Folia clin. int.* (*Barcelona*)] **5**, 1–5, Jan., 1955.

This paper, which comes from Stockholm, presents a short review of the senior author's recent results in performing total hypophysectomy with the object of limiting the growth of malignant tumours with metastases, or of providing additional control of malignant diabetes mellitus. Many tables of results are given [but for a technical description of their methods the authors refer the reader to the *Journal of Neurosurgery*, omitting, however, to give any bibliographical references].

They first discuss the results in mammary carcinoma, for which 37 patients have been subjected to hypophysectomy since February, 1954. Of these, 7 were excluded from the statistics, 4 because of incomplete operation and 3 because of postoperative death from other causes, such as pulmonary embolism. Of the remaining 30 patients, 14 were reported to be alive and 16 had died; of 7 with known cerebral or hepatic metastases, only one was surviving at the time of writing. No hormonal therapy was given before operation or during the postoperative period, but on leaving hospital patients received 25 mg. of cortisone and an amount of thyroid extract equivalent to 100 mg. of thyroxine per day. In general the results were rather better in the younger patients, up to the age of 55. The authors also describe 2 cases of prostatic carcinoma in which hypophysectomy gave encouraging results.

In the second group of cases 10 diabetic patients, 5 males and 5 females aged 23 to 30 years, underwent the operation. All had severe ocular and renal complications, but 6 survived the operation for periods of between 6 months and 2 years at the time of writing. The sensitivity to insulin was greatly increased, rendering the development of hypoglycaemia a danger postoperatively. Cortisone in doses of 5 to 10 mg. per day and thyroid as for the cancer cases, were also given. In these cases the operation was considered to be life-saving. *Donald McDonald*

1356. **Determination of Osmotic Pressure in Diabetes Insipidus. A New Diagnostic Test**
L. S. DREIFUS, M. N. FRANK, and S. BELLET. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 1091–1094, Dec. 30, 1954. 2 figs., 14 refs.

A new test for the diagnosis of diabetes insipidus, which should be particularly useful in the differentiation of this condition from psychogenic polydipsia with polyuria, is described in this paper from the Philadelphia General Hospital. It consists simply in estimation and comparison of the osmotic pressures of the blood and urine, and is based on the fact that in diabetes insipidus the kidney is unable to elaborate a urine that is hypertonic to the blood but is able to do so when exogenous hormone is administered. The test is performed after withholding food and water for 3¼ hours, osmotic pressures being measured by the depression of the freezing point with a Beckman type of thermometer. In 4 untreated cases of diabetes insipidus it was found that the ratio of osmotic pressure of urine to that of the blood was always less than 1; after intravenous injection of 5 pressor units of "pitressin" the ratio rose to more than 1. *Nigel Compston*

THYROID GLAND

1357. **Muscular Disorders in Hyperthyroidism.** (Muskuläre Störungen bei der Hyperthyreose)
H. PIPBERGER, R. KÄLIN, and T. WEGMANN. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **85**, 390–393, April 23, 1955. 3 figs., 44 refs.

The authors classify the muscular disorders of hyperthyroidism according to the frequency of their occurrence as follows: (1) chronic hyperthyrotic myopathy; (2) myasthenia gravis pseudoparalytica; (3) paroxysmal paralysis; (4) exophthalmic ophthalmoplegia. The clinical picture and pathology of each of these conditions are discussed briefly with reference to the authors' own series of 13 cases seen at the Medical Polyclinic of the University of Zürich. Complete laboratory investigations were supplemented in some cases by muscle biopsy, and in all cases by electromyography of at least two of the principal muscles of the arm and of the leg. In 9 cases there was a definite reduction in muscular power, while in 12 of the 13 electromyographic changes indicative of muscular dystrophy were found in at least one muscle. The authors point out that the condition is likely to be overlooked, or misdiagnosed as a primary neuromuscular disorder. *V. C. Medvei*

1358. **Muscular Disorders in Hypothyroidism.** (Muskuläre Störungen bei der Hypothyreose)
H. PIPBERGER, R. KÄLIN, and T. WEGMANN. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **85**, 420–423, April 30, 1955. 4 figs., 36 refs.

Muscular disorders associated with hypothyroidism were first described in 1897 by Hoffmann, by whose name the syndrome is sometimes known. In the majority of cases the volume of the muscle is increased and the signs are those of a muscular hypertrophy, while in some there is evidence of muscular dystrophy. The authors discuss 5 cases (in 4 women and a man, aged 42 to 62) which they have observed at the Medical Polyclinic of the University of Zürich. These patients had no diminution of motor power, though painful

spasms and myotonoid response were observed. The result of muscle biopsy in 2 cases was normal. There was no creatinuria, although creatine metabolism was slightly abnormal. Electromyograms were abnormal in all cases, with a prevalence of signs of hypertrophy.

V. C. Medvei

1359. **Cortical Control of the Thyrotrophic Function of the Hypophysis and of Thyroid Function.** (Кортикальная регуляция тиреотропной функции гипофиза и щитовидной железы)

Y. B. SKEBELSKAYA. *Проблемы Эндокринологии и Гормонотерапии* (*Probl. Endokr. Gormonoter.*] **1**, 9–15, No. 2, March–April, 1955. 2 figs., 6 refs.

At the All-Union Institute of Experimental Endocrinology, Moscow, 274 male rats were subjected to experiments involving the formation of conditioned reflexes to the administration of thyroxine and methylthiouracil, the conditioning stimulus in both cases being the procedure of administration itself combined with switching on of an electric light or, in the case of orally administered methylthiouracil, smearing of the animal's mouth with 1% hydrochloric acid. The unconditional stimulus was given daily for 10 days after which it was replaced by similarly administered normal saline solution or distilled water. Three series of experiments were conducted, lasting 22, 32, and 44 days respectively. Reinforcement of the conditioned reflex was required every 5 to 7 days for its perpetuation.

The conditioned reflex established to administration of thyroxin and methylthiouracil had the same effect as the actual drug itself on the weight of the thyroid gland, the thickness of its epithelium, the uptake of radioactive iodine, and the amount of thyrotrophic hormone in the pituitary gland. The animals in the control group receiving the same number of injections of thyroxine but without the conditioning stimulus, did not develop a conditioned reflex and in them the hypophysial concentration of thyrotrophic hormone differed little from normal.

A. Swan

1360. **The Significance of the Higher Nervous Centres in the Reaction to Thyrotrophic Hormone.** (Значение нервной системы и ее высших отделов в реакции на тиреотропный гормон)

P. A. WUNDER. *Проблемы Эндокринологии и Гормонотерапии* (*Probl. Endokr. Gormonoter.*) **1**, 15–20, No. 2, March–April, 1955. 1 fig.

The author describes a series of three experiments undertaken at the University of Saratov on chicks, white mice, and marmots in order to elucidate the role of the higher nervous centres in the reaction of the thyroid gland to thyrotrophic hormone.

(1) A conditioned reflex was established in intact animals to the administration of thyrotrophic hormone. The return to the basal state in these conditioned animals, as estimated by the weight of the thyroid, the height of its epithelium, and the diameter of the follicles—even without reinforcement of the conditioned reflex—took a significantly longer time than in non-conditioned animals.

(2) In the second experiment the effect of administration of caffeine was studied. It was found that caffeine alone produced stimulation of the thyroid gland. However, when administered in conjunction with thyrotrophic hormone the combined effect of the two drugs was not only not enhanced, but an apparent mutually antagonistic suppressive action was observed.

(3) The effect of thyrotrophic hormone was studied in chicks after (*a*) trephining of the skull, (*b*) removal of one cerebral hemisphere, and (*c*) removal of both cerebral hemispheres. After the first two operations the results were inconclusive, but after the removal of both hemispheres the effects of thyrotrophic hormone were greatly enhanced.

It is claimed that these experiments demonstrate that, apart from its direct action on the thyroid gland, thyrotrophic hormone acts also through the central nervous system.

A. Swan

See also Pathology, Abstract 1201.

ADRENAL GLANDS

1361. **Eosinophil Response to Graded Doses of ACTH and Cortisone in Man**

A. T. MILLER *Journal of Applied Physiology* [*J. appl. Physiol.*] **7**, 663–665, May, 1955. 7 refs.

Studies at the University of North Carolina have shown the eosinophil count to be superior to other commonly used indices of adrenocortical response to single injections of ACTH. The present study was designed to provide the basis for a more detailed analysis of the factors influencing the eosinophil response to both ACTH and cortisone. To 20 healthy male dental students ACTH was given intramuscularly in doses of 5, 10, and 20 *U.S.P.* units, and cortisone acetate was given orally in doses of 12·5, 25, and 50 mg. In every case the drug or a control saline injection was given at noon, and eosinophil counts were made at 8.0 a.m., noon, and 4.0 p.m. There was an interval of at least one week between successive tests, each subject being tested twice at each dose level of ACTH and cortisone.

The threshold dose for intramuscular ACTH was found to be less than 5 units and for oral cortisone less than 12·5 mg. For ACTH, in the dose range 0 to 10 units, the eosinophil response was found to distinguish between doses differing by 5 units, and in the dose range 10 to 40 units to distinguish doses differing by 10 units. The author points out that the minimum difference in dose detectable in this way increases with increasing dose because of the asymptotic approach to complete depression of the circulating eosinophil count. The minimum difference in dose that could be detected in the case of cortisone was of the order of 12·5 mg. over the whole range from 0 to 50 mg., the dose–response relationship being almost perfectly linear over this range.

In discussion the author suggests that from these findings it would appear that the eosinophil response to hormonal stimulus is not merely superimposed upon a diurnal trend, but that the diurnal trend is actually

abolished by the administration of hormone. Thus strict standardization of tests to correct for directional changes in the eosinophil count during the period before testing does not appear to be necessary.

Adrian V. Adams

1362. **Studies on the Antipyretic Action of Cortisone in Pyrogen-induced Fever**

E. Atkins, F. Allison, M. R. Smith, and W. B. Wood. *Journal of Experimental Medicine* [*J. exp. Med.*] **101** 353–366, April 1, 1955. 6 figs., bibliography.

In this study of the antipyretic action of cortisone, carried out at Washington University School of Medicine, St. Louis, fever was induced in male rabbits weighing 2·5 to 3·5 kg. by means of " pyromen ", a highly purified polysaccharide from a species of *Pseudomonas*, or of native dextran with an average molecular weight of between 200,000 and 300,000, or by injecting typhoid vaccine. One group of animals received 25 mg. of cortisone twice daily for the 3 days preceding the experiment, another group remaining untreated as a control. On the day of the experiment the treated group received a further injection of 25 mg. of cortisone, and both groups were then given pyromen. In both groups there was a transient fall in the leucocyte count, but only the control group showed a significant rise in temperature. In a repetition of the experiment using dextran as the pyrogen a similar result was obtained.

Two experiments were then carried out to test whether the serum factor known to be involved in the action of pyrogens was affected by cortisone. In the first typhoid vaccine incubated with serum from cortisone-treated rabbits was injected into rabbits made tolerant to this pyrogen. The latent period of the response was identical with that in tolerant rabbits given typhoid vaccine incubated with normal serum, thus showing that pretreatment of an animal with cortisone did not eliminate the serum factor. In the second experiment the injection of typhoid vaccine incubated with normal serum did not produce fever if the rabbits had previously been treated with cortisone. The authors conclude that the antipyretic effect of cortisone does not involve the leucopenic reaction nor the fever-accelerating factor present in the serum.

P. A. Nasmyth

1363. **Intravenous Hydrocortisone**

J. D. N. Nabarro. *Archives of the Middlesex Hospital* [*Arch. Middx Hosp.*] **5**, 79–86, April, 1955. 5 figs., 11 refs.

It is first pointed out that in the treatment of acute adrenal insufficiency, when it is necessary rapidly to raise the level of circulating hormone, intravenous administration of hydrocortisone is much more effective than intramuscular. Though it has no advantage over oral administration of cortisone, which is followed within an hour by a significant rise in the plasma level of 17-hydroxycorticosteroids, it may be necessary for the patient who is unconscious or vomiting. The author describes the results of intravenous infusion of hydrocortisone in 2 cases of Addisonian crisis, one case of acute adrenal insufficiency during adrenalectomy, one of adrenal insufficiency after operation following prolonged cortisone therapy, in one of severe post-operative shock, and in one of Cushing's syndrome as a diagnostic test to distinguish between adrenal tumour and hyperplasia.

In the 2 cases of Addisonian crisis the results were disappointing, and this is attributed partly to the fact that the solution was made up in 5% glucose and not normal saline and partly to the fact that no additional cortisone was given by mouth or intramuscular injection. Hydrocortisone for intravenous use is supplied in ampoules containing 100 mg. in 20 ml. of 50% alcohol, this being added to 0·5 or 1·0 litre of an isotonic fluid. Usually the Addisonian crisis is associated with sodium depletion and the diluent should therefore be normal saline. Since the effect of intravenous hydrocortisone is transient, the level of circulating hormone falling rapidly at the end of the infusion, it is necessary to give cortisone intramuscularly as well and to continue the infusions until this becomes effective or oral administration is possible. The author suggests the following regimen for the treatment of patients in Addisonian crisis. If the patient can take cortisone by mouth 100 mg. should be given every 4 hours until improvement is obvious; in other cases 100 mg. of cortisone should be given intramuscularly and an infusion of hydrocortisone in normal saline begun. For the first 2 hours the rate of infusion should be 25 mg. an hour; subsequently it should 12·5 mg. an hour. The infusion should be continued for at least 8 hours, and as soon as possible cortisone should be given by mouth. In cases in which the plasma potassium level is very high an intramuscular injection of 5 to 10 mg. of deoxycortone is advisable.

Acute adrenal insufficiency in which there is no sodium depletion may occur during operation or when a patient with adrenal atrophy is subjected to severe stress. Two such cases are described, in both of which there was a satisfactory response to intravenous infusion of hydrocortisone in 5% glucose.

Rukes *et al.* (*Metabolism*, 1954, 3, 481) reported cases of severe surgical shock uninfluenced by blood or plasma transfusion or by noradrenaline which responded to intravenous infusion of hydrocortisone. In one case of this type in the present series benefit was only temporary. The author suggests that the use of hydrocortisone in such cases merits further investigation.

Kenneth Stone

1364. **Cytomegaly of the Adrenal Gland**

E. C. Beatty and C. R. Hawes. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 463–467, April, 1955. 3 figs., 15 refs.

At birth the human adrenal gland is about one-third as large as the kidney—the adult gland is only one-thirteenth—the cortex is notably thick, and only its outer fifth is of the adult type, the remainder, which undergoes degeneration in the 7 or 8 weeks of involution following birth, being " foetal " in type. Cytomegaly of this foetal layer has been described, but little is known of the phenomenon. The authors have therefore re-

examined the pathological reports and tissue sections in 1,243 necropsies carried out between 1942 and 1953 at the Children's Hospital, Denver, Colorado, half of which were on infants aged 6 months or less; in this group 11 cases of cytomegaly of the gland were discovered.

All the cases were in infants of Caucasian stock, 6 being female and 5 male, who ranged in age from 3 hours to 4 months. Single or multiple congenital anomalies were present in 9 of the cases, but were clinically apparent in only 5; they included epidermolysis bullosa, polydactylism, hemihypertrophy, complex cardiac anomalies, multicystic kidneys, stricture of the ureter, macroglossia, omphalocele, fibrocystic disease of the pancreas, hyperplasia of pancreatic islet tissue, Meckel's diverticulum, and diaphragmatic hernia—all of which can be related to processes occurring between the 5th and 7th weeks of foetal life. Clinically, in 5 cases there had been severe dehydration due to persistent vomiting or non-infective diarrhoea, or both.

The gross appearance and the general microscopic architecture of the adrenal glands were normal, and the diagnosis was established by the discovery of large cells, 20 to 100 μ in diameter, occurring singly or in groups in some areas of the foetal-type cortex or at the junction with the adult-type cortex. Their nuclei were large and hyperchromatic, and some contained vacuoles; the cytoplasm was granular and often contained a more coarsely granular inclusion body. No evidence of cytomegaly or inclusions was found in any other organ.

The entity has no known relation to any viral disease in the mother and probably no relation to the cytomegalic inclusion disease of infancy which affects the salivary glands. The true incidence of the condition is not known. *T. B. Begg*

1365. **Studies in Phaeochromocytoma: III. The Excretion of Noradrenaline in the Urine of Cases of Hypertension and its Value in the Diagnosis of Phaeochromocytoma**

G. B. West and N. R. W. Taylor. *Glasgow Medical Journal* [*Glasg. med. J.*] **36**, 123–129, April, 1955. 2 figs., 12 refs.

The authors, working at Queen's College, Dundee, describe extensive studies of the urinary excretion of pressor amines in cases of hypertension and of phaeochromocytoma.

A significantly high output of catechol amine was observed in only 3 out of 32 hypertensive patients who gave a positive reaction to one of many pharmacological screening tests for phaeochromocytoma, and all 3 were later found to have an active adrenal tumour. The urinary excretion of noradrenaline was below 60 μg. per 24 hours in 169 of 200 hypertensive patients, values up to 80 μg. per 24 hours being observed in 31. In the 3 cases of phaeochromocytoma the urinary excretion of noradrenaline was between 225 and 750 μg. per 24 hours; after operation it returned to normal, a finding considered to be important since it excludes the possibility of multicentric foci. It was also found that the pressor amine content of the adrenal glands of hypertensive patients was slightly higher than that of controls.

The authors recommend bioassay methods for measuring noradrenaline [for which the original paper should be consulted]. It is concluded that an increased urinary output of noradrenaline is diagnostic of the presence of a phaeochromocytoma.

J. N. Harris-Jones

1366. **Phaeochromocytoma and Neurofibromatosis. Adrenolytic Effect of Phentolamine and Chlorpromazine**

J. Knox and A. Slessor. *Lancet* [*Lancet*] **1**, 790–794, April 16, 1955. 5 figs., 27 refs.

The association of chromaffin tumours with neurofibromatosis was first noted by Rosenthal and Willis in 1936, and the incidence of neurofibromatosis among published cases of phaeochromocytoma is about 5%. In this paper from the University of Glasgow the authors describe a case of neurofibromatosis in a man of 40 in which the presence of a phaeochromocytoma was suspected on account of hypertension associated with sudden attacks of dizziness and throbbing frontal headache. When first seen the patient's blood pressure was 170/120 mm. Hg, and he had the typical subcutaneous nodules of neurofibromatosis. An intravenous injection of 0·025 mg. of histamine provoked an attack in which the blood pressure rose to 260/150 mm. Hg, with marked symptoms of headache and anxiety. An intravenous injection of phentolamine (" rogitine ") given when the blood pressure was 150/100 mm. Hg caused an immediate fall of 30 mm. Hg in both the systolic and diastolic levels. There was increased urinary excretion of catechols, and a radiograph showed a plaque of calcification above the left kidney, indicating the probable site of the tumour. This was confirmed at operation, when a phaeochromocytoma was found and excised. Despite the administration of 10 mg. of phentolamine there were two hypertensive phases during the operation, whereas after excision of the tumour the blood pressure fell to 90/60 mm. Hg and a drip infusion of noradrenaline was necessary during the first 30 hours to maintain the pressure at a reasonable level.

Since the operation the patient has had occasional attacks of dizziness without headache, and the blood pressure has ranged from 140/100 to 165/120 mm. Hg. It is therefore considered possible that another phaeochromocytoma is present. For anaesthesia, chloroform, ethyl chloride, and cyclopropane are contraindicated in operations for phaeochromocytoma as they are liable to produce ventricular fibrillation in the presence of excess circulating adrenaline. Tubocurarine was used in the operation on this patient, but was thought to produce a rise of blood pressure, possibly through its release of histamine.

It is noted that whereas premedication with phentolamine and chlorpromazine much reduced the severity of the symptoms provoked by the intravenous injection of histamine, it did not prevent the rise in blood pressure. This presumably indicates that while these drugs have a strong adrenolytic action, they have little blocking action on noradrenaline. *G. S. Crockett*

See also Pathology, Abstract 1198.

The Rheumatic Diseases

1367. **Severe and Prolonged Haematemesis in the Course of Treatment with Phenylbutazone.** (Hématémèse grave et prolongée au cours d'un traitement par la phénylbutazone)
R. MOREAU, R. CLER, and R. PEROL. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **71**, 97–100, Feb. 11, 1955.

Phenylbutazone is an analgesic which has been used for the treatment of rheumatism and conditions such as osteoarthritis. Its use, however, is sometimes accompanied by toxic side-effects, the most serious being haemorrhage from the gastro-intestinal tract. The present authors record in detail the case of a woman of 29 who had had rheumatoid arthritis as a child and occasional transitory arthritis subsequently. She had recently consulted her doctor because of a more persistent pain in the lumbar region, for which she was given phenylbutazone, a total dose of 2·9 g. being taken over a period of 5 days (250 mg. on the first day, 850 mg. on the second day, and 600 mg. for each of the 3 following days). On the second day of treatment she experienced burning epigastric pain and her stools were black. On stopping treatment the epigastric pain disappeared, but 6 days later she had a severe haematemesis and for the next 12 days her condition remained serious in spite of blood transfusions and other treatment. Radiological examination of the stomach did not establish the presence of an ulcer with any certainty. The patient eventually made a good recovery. *R. Wien*

1368. **Haemorrhage from the Digestive Organs during Treatment with Phenylbutazone.** (Les hémorragies digestives au cours des traitements par la phénylbutazone)
F. COSTE, B. ANTOINE, and S. RAMPON. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **71**, 100–114, Feb. 11, 1955. 4 figs., 11 refs.

Four cases of gastro-intestinal haemorrhage following the administration of phenylbutazone are reported. In the first the patient had an extremely painful neuralgia in the left cervico-brachial region (subsequently shown to be due to neoplastic destruction of a cervical vertebra). Treatment, which included 500 mg. of phenylbutazone given by intramuscular injection daily, produced much relief of the pain, but after 2 weeks the patient developed severe melaena and shock, with anaemia which persisted in spite of blood transfusions. After a haematemesis 2 weeks later gastric and duodenal ulcers were demonstrated radiologically and the patient died after gastrectomy. The second patient was treated for rheumatoid arthritis with phenylbutazone in a daily dose of 400 mg. by mouth for 11 days, followed by 600 mg. daily for another 2 weeks. This improved the condition considerably, but was followed by a haemorrhage of fresh blood per rectum which stopped immediately on withholding phenylbutazone. Proctoscopy and radiological examination of the gastro-intestinal tract revealed no abnormality. Two weeks later aspirin was given for a recurrence of the arthritic pains and a similar haemorrhage occurred without any subsequent ill-effects. The third patient developed melaena after receiving phenylbutazone intramuscularly for lumbar osteoarthritis in a dose of 1 g. every 2 days for 20 days; it was not possible to determine the source of the haemorrhage. The fourth patient was treated for sciatica with phenylbutazone in a daily dose of 800 mg. by mouth. After 10 days of treatment blood appeared in the stools and the patient complained of severe gastric pain. *X*-ray examination showed signs of gastritis which cleared up when treatment with phenylbutazone was stopped.

In an attempt to elucidate the effect of phenylbutazone on the gastro-intestinal tract the stools of 41 patients suffering from various types of rheumatic and arthritic conditions were tested for blood by the amidopyrine method after oral treatment with phenylbutazone in daily doses of 0·4 to 1 g. for an average period of 49 days. Whereas in all cases the test had given negative results before treatment, a positive result was obtained repeatedly after treatment in 15 cases and intermittently in 11 others. The occurrence of blood appeared to be related to the duration of treatment in most cases, but in some blood was present after a relatively short course of treatment. Although the authors admit that pre-existing factors may have determined the occurrence of severe haemorrhage in the 4 cases described, it would appear probable from their later experimental findings that some action of phenylbutazone was at least a contributory factor. *R. Wien*

1369. **Clinical and Experimental Studies on the Pathogenesis of the Gastric Lesions (Ulcers, Haemorrhages) Provoked by Phenylbutazone.** (Considérations cliniques et expérimentales sur la genèse des lésions gastriques (ulcères, hémorragies) provoquées par la phénylbutazone)
S. BONFILS, J. P. HARDOUIN, C. RICHIR, F. DELBARRE, and A. LAMBLING. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **71**, 114–124, Feb. 11, 1955. 4 figs., 7 refs.

It was found by the authors that gastric lesions could be produced experimentally in the rat by giving daily doses of 100 mg. of phenylbutazone per kg. body weight, either by mouth or by injection, after ligating the pylorus. These lesions, which appeared about the sixth day, took the form of small, diffuse ulcers, often haemorrhagic, originating in the mucous glandular layer and extending towards the surface. Concomitantly there was a considerable fall in the hydrochloric acid content of the gastric juice, resulting in some cases in achlorhydria. Analysis of the gastric juice showed that little phenylbutazone was excreted by this route.

The lesions produced clinically and experimentally by phenylbutazone are contrasted with those associated with the clinical administration of cortisone and ACTH. The latter occur in the duodenum rather than the stomach, and are the result of increased gastric secretion and hyperchlorhydria, whereas the appearance of the experimental lesions suggests that phenylbutazone has a direct toxic action on the gastric mucosa. There is thus little support for the suggestion that the gastric effects of phenylbutazone treatment are due to stimulation of the adrenal cortex. *R. Wien*

See also Pathology, Abstract 1186.

1370. **Failure of ACTH in Acute Rheumatism as a Result of Recurrent Streptococcal Infection.** (Über das Versagen von ACTH beim akuten Rheumatismus infolge rezidivierender Streptokokkeninfektionen)
E. F. PFEIFFER and K. SCHÖFFLING. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] **14**, 88–94, April, 1955. 1 fig., bibliography.

The authors describe 2 cases seen at the University Medical Clinic, Frankfurt-am-Main, which illustrate the danger of hormone therapy in the presence of streptococcal infection. Both patients had rheumatic fever with tonsillitis, and in both the administration of ACTH (corticotrophin) controlled the polyarthritis for a time. An acute exacerbation then took place in the tonsillitis and the condition of the joints relapsed once more. Antibiotics usually clear up an attack of tonsillitis very quickly, but failed to do so in these patients, even in high dosage. Evidence of cardiac damage was present in both cases.

The authors stress that in cases of acute rheumatism antibiotic treatment for associated tonsillitis should be carried out as early as possible, and if the throat infection persists tonsillectomy should be considered; it may thus be possible to avoid this particular complication of hormone therapy. In 3 other cases observed at the same time the tonsillitis had completely subsided before treatment with ACTH was begun and in these cases no complication was encountered. *David Preiskel*

RHEUMATOID ARTHRITIS

1371. **Rheumatoid Arthritis in Childhood**
W. M. FYFE. *Glasgow Medical Journal* [*Glasg. med. J.*] **36**, 102–110, March, 1955. 3 figs., 8 refs.

The clinical records and the results of a follow-up investigation of 72 children (30 males and 42 females) with rheumatoid arthritis admitted to the Royal Hospital for Sick Children, Glasgow, since 1930 are reviewed. In 30 cases the age at onset of the disease was 5 years or less. The joint involvement was usually bilaterally symmetrical and muscle atrophy developed rapidly. Transient skin rashes were noted in 18 cases and psoriasis was present in 4 others. Adenopathy developed in 36 cases during the illness, accompanied by splenomegaly in 10. In 5 cases, 2 of which were fatal, there were features of both rheumatoid arthritis and rheumatic fever.

Of the 72 patients, 56 were traced, 49 of these being re-examined. The disease was quiescent—that is, there had been no joint pain and tenderness for at least 2 years—in 34 patients. Of these, 22 made a complete recovery, 5 were moderately crippled, 5 severely crippled, and 2 were only mildly disabled.

The value in treatment of ACTH, cortisone, vitamin D_2, gold injections, salicylates, and tonsillectomy is discussed; it is concluded that recovery is not related to any particular form of treatment given. *Kathleen M. Lawther*

1372. **Treatment of Rheumatoid Arthritis with Cortisone. (Two- to Four-year Studies.)** [In English]
K. B. HANSEN, F. FISCHER, and K. BRØCHNER-MORTENSEN. *Acta rheumatologica Scandinavica* [*Acta rheum. scand.*] **1**, 7–21, 1955. 4 figs., 15 refs.

A further study of the long-term treatment of rheumatoid arthritis with cortisone is presented from Rigshospitalet, Copenhagen, with special reference to adrenocortical activity after such treatment. The series studied consisted of 50 cases of rheumatoid arthritis in 15 males and 35 females ranging in age from 30 to 50 years. The more severe type of case preponderated. Treatment was initiated with ACTH (corticotrophin) in order to determine the initial 17-ketosteroid excretion response, and was then continued with cortisone [presumably by mouth] at a maintenance dosage of 50 to 75 mg. daily, the level being determined by the patient's tolerance rather than by remission of symptoms. All other treatment was discontinued and the use of analgesics was avoided as far as possible.

In 19 cases adrenocortical function was re-assessed after 9 to 41 months of continuous cortisone therapy by determining the rate of urinary excretion of 17-ketosteroids following the administration of ACTH in doses of 20 units 6-hourly. Before treatment the average increase in 17-ketosteroid excretion was 100%. During treatment the average basal rate of excretion fell by 40%, but stimulation with ACTH after a long period of cortisone therapy resulted in a rise in 17-ketosteroid excretion to an average of 420% of the pre-stimulation value and 250% of the pre-treatment value. The mode of response after cortisone therapy varied, the patients falling into 3 groups according to the rapidity of the response, but the type of response appeared to be unrelated to age, sex, clinical condition, or dosage and duration of cortisone therapy. The decrease in adrenocortical function induced by prolonged cortisone therapy is therefore shown to be readily reversible on stimulation with ACTH.

From the clinical aspect, complete remission was induced in 3 cases, "considerable improvement" in 19 cases, "some improvement" in 15, and none in 13 patients. In 16 of the 50 cases treatment was discontinued on account of an unsatisfactory response or the development of complications. Of the remaining 34 patients, the number totally incapacitated fell from 8 to 1, while the number of those able to work increased from 2 to 21. Some undesirable side-effects were noted in practically all cases. Mental disturbance occurred in 11 patients, but with no permanent damage. Two cases of gastric ulcer are recorded, and 2 deaths from pneumonia.

It is concluded that prolonged treatment with cortisone has proved of value in more than half the cases studied, and is indicated in cases where the disease progresses actively despite the application of other methods of control or in very active cases in order to inhibit progress before irreversible joint changes can occur. The patient should be kept continually under observation, and particular care taken to increase the dosage of cortisone rather than to stop treatment on the occurrence of infection, trauma, or acute surgical emergencies.

Harry Coke

COLLAGEN DISEASES

1373. The Natural History of Systemic Lupus Erythematosus: an Approach to its Study through Chronic Biologic False Positive Reactors

J. E. MOORE and W. B. LUTZ. *Journal of Chronic Diseases* [*J. chron. Dis.*] **1**, 297–316, March, 1955. 1 fig., 11 refs.

In 1948 an investigation was begun at Johns Hopkins University and Hospital, Baltimore, the aims of which were (1) to investigate the validity of the treponemal immobilization (T.P.I.) test, and (2) to study the phenomenon of " biologic false positivity ". In this paper the authors are mainly concerned with the second point, but they briefly quote the work of Zellmann, who concluded that a negative T.P.I. reaction differentiates between a syphilitic infection and a biological false positive (B.F.P.) reaction with a margin of error of about 2%, provided treated early syphilis and definite clinical evidence of syphilis are excluded.

B.F.P. reactions may be " acute " or " chronic "; the acute reaction occurs shortly after an acute infectious illness, and usually disappears within 6 months. The aetiology of the chronic reaction was in 1948 almost completely unknown, but in the intervening 6 years the authors have studied 148 chronic B.F.P. reactors, of whom 104 (70%) were female. When first seen only 4 patients were suffering from overt disease which might have been related to the phenomenon, while of the remainder, two-thirds had no symptoms at all and one-third had only minor symptoms which were not obviously relevant. In all cases the standard serological tests for syphilis had been positive for at least one year.

However, during the period of observation 10 patients developed definite systemic lupus erythematosus, 7 developed rheumatoid arthritis (which may be the first manifestation of systemic lupus erythematosus), and 45 were tentatively diagnosed as possible or probable cases of lupus erythematosus on clinical grounds, though without pathological confirmation. The most common clinical features of systemic lupus erythematosus, as seen in this series, are tabulated, short clinical histories of representative patients are given, and the positive laboratory findings are briefly described. Mild anaemia was fairly common in the female patients, but leucopenia was unusual. Chemical and electrophoretic tests on the serum proteins showed some abnormality of the globulin fraction in 90% of the cases. In over half the cases the erythrocyte sedimentation rate was persistently raised. It is also noted that the reaction was first observed when half the female patients and one-quarter of the males were under the age of 25. It is suggested that the finding of a B.F.P. reaction should be an indication for a search for the cause.

The clinical course of systemic lupus erythematosus developing under these circumstances appears to be exceedingly chronic, compared with the usual picture of the disease. It is hoped that continuation of this study over a further period of years will give a more accurate picture of the natural history of this disease than can be obtained from the retrospective study of advanced cases.

Nigel Compston

1374. Viscero-cutaneous Collagenosis. A Study of the Intermediate Forms of Dermatomyositis, Scleroderma, and Disseminated Lupus Erythematosus

W. PAGEL and C. S. TREIP. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 1–18, Feb., 1955. 22 figs., 42 refs.

The close relationship between dermatomyositis and scleroderma has been recognized for some years. In scleroderma associated visceral lesions are so common that the term " progressive diffuse sclerosis " has been suggested. The present authors, writing from the Central Middlesex Hospital, London, consider that the clinical and histological features of dermatomyositis, progressive diffuse sclerosis, and disseminated lupus erythematosus, may overlap sufficiently to render differential diagnosis impossible in some cases, and they therefore suggest an even more general term—namely, " viscero-cutaneous collagenosis ".

Seven cases are described in detail and excellent photomicrographs are reproduced. One patient in whom dermatomyositis was diagnosed died 11 years later from a condition in which the lesions resembled those of progressive diffuse sclerosis; it would seem that these two conditions are stages in the same disease. At necropsy on 2 cases clinically resembling dermatomyositis there were histological skin changes of scleroderma. In another case of scleroderma of 20 years' duration some histological changes of dermatomyositis and disseminated lupus erythematosus were found. The clinical diagnosis of polyarteritis nodosa in another case was not substantiated at necropsy, the features observed being common to disseminated lupus erythematosus, dermatomyositis, and progressive diffuse sclerosis.

The authors state that the changes in the nail fold clinically regarded as characteristic of disseminated lupus erythematosus and dermatomyositis consist in patchy extravascular fibrinoid necrosis associated with capillary thromboses—an unusual combination of collagen disease and acronecrosis. Focal necrosis and focal fibrosis respectively in the adrenal glands in 2 cases of dermatomyositis were considered to be early and late stages of the same process.

[For the detailed description of the histological findings in these cases the original paper should be consulted.]

Nigel Compston

See also Pathology, Abstract 1221.

Physical Medicine

1375. **Changes in Heart Rate during Exposure of the Skin to Radiant Heat**

K. E. Cooper and D. M. Kerslake. *Clinical Science [Clin. Sci.]* **14**, 125–135, Feb., 1955. 8 figs., 8 refs.

In this paper from St. Mary's Hospital, London, and the R.A.F. Institute of Aviation Medicine, Farnborough, Hants, the authors describe experiments in which it was found that when subjects were exposed to radiant heat there was an increase in the heart rate without change in blood pressure. Heat was supplied by six 100-watt electric light bulbs arranged in a metal reflector cradle over the subject. Skin temperature was measured by an intradermal thermocouple and precautions were taken to eliminate errors due to heat conduction. Oral temperature was measured by a clinical thermometer, and rectal temperature by a thermocouple inserted into the rectum to a depth of 4 to 6 inches (10·2 to 15·2 cm.). Blood pressure was recorded by means of a clinical sphygmomanometer on the arm.

During heating of the trunk the heart rate increased rapidly at first and then more slowly, falling abruptly on cessation of heating; the buccal, oesophageal, and rectal temperatures fell for about 10 minutes, then rose slowly. There was no significant change in blood pressure. When the legs were heated during application of an arterial tourniquet the heart rate increased; no increase in heart rate was observed if the tourniquet was applied without heating. There was a positive correlation between the degree of heating and the heart rate, but no correlation between the change in heart rate and in the temperature in the mouth.

The authors conclude that there is a neural link between thermal receptors in the skin and the centres controlling the heart rate, and that increase in the latter is not due to a rise in the temperature of blood going to the brain or in the blood pressure. *J. B. Millard*

1376. **Electrodiagnosis in Motor Unit Dysfunction**

P. Bauwens. *Proceedings of the Royal Society of Medicine [Proc. roy. Soc. Med.]* **48**, 194–200, March, 1955. 4 figs., 3 refs.

In discussing the principles of electrodiagnosis of dysfunction in a motor unit the author recalls that in normal conditions a nervous impulse arising in the anterior horn cell of the cord causes all muscle fibres composing the unit to be excited almost simultaneously, and their concerted activity produces a diphasic or triphasic electrical potential of 3 to 10 milliseconds' duration. If, however, for any reason there is delay on the part of some fibres to contribute to the electrical effect a temporal dispersion may take place, resulting in a more complex and less compact pattern in the electromyogram. On the other hand, if a considerable number of muscle fibres within the unit fail to respond at all, the resultant electrical pattern will be of low amplitude and shorter duration; this is the electromyographic pattern of the classic dystrophies, but is not confined to them since it may also be seen in the secondary myopathies associated with thyrotoxicosis and other disorders, and even in some cases of myasthenia gravis. In such conditions there is no evidence of actual denervation, nor is there any fibrillation. There is, however, a group of conditions in which this "myopathic pattern", as the author terms it, may co-exist with signs of partial denervation; this combination can be explained by assuming that a neuronitis causes degeneration of the terminal portion of some of the axon branches, as occurs in such conditions as polyneuritis, neuromyositis, and certain cases of dermatomyositis.

In the neuropathies the functional disorder is that of the motor unit itself, and the electromyographic result of this is a simplification of the interference pattern on volition. These neuropathies show signs of frank denervation. It might appear that the electrical pattern produced by involvement of the motor neurone in the anterior horn should not be dissimilar to that due to involvement of the nerve root or trunk, but in fact there are certain distinctive electrodiagnostic features, the most striking of which is the discrepancy between the relatively normal response of the muscle to electrical stimulation of the nerve and the abnormal electromyographic pattern elicited by voluntary movement of the muscle. On volition, instead of the relatively slow build-up of the normal pattern, discrete, large-amplitude motor-unit potentials may make an immediate appearance. Moreover, only a single repetitive potential may be picked up. Occasionally polyphasic potentials, not unlike those seen in the myopathies, may be obtained, but such patterns seem to occur in compact trains rather than as continuous patterns. (Electromyograms illustrating this are reproduced.) Fasciculation and fibrillation potentials are common at rest, but frank denervation is seen only in the very late stages.

In discussing the theoretical background to these findings in the myelopathies the author advances as a possibility the idea that a disturbance of the muscle "servo-mechanism" is responsible for these large, discrete motor-unit potentials. It is generally accepted, he states, that the link between a muscle and the appropriate segment of the cord comprises at least one afferent and two efferent neurones. One of these efferents, acting as a primer to the intrafusal fibres, sets in motion the afferent part of the loop, which then relays the information to the anterior horn cell, and this initiates the contraction of the muscle. This cybernetic system can be short-circuited when urgent, less precise, action is required. If then the primary mechanism fails, muscle movement will be produced only by direct paths, and such movement might produce the electromyographic pattern characteristic of the myelopathies. It has been shown experimentally that de-afferentation does indeed produce such an electromyogram. *L. A. Liversedge*

Neurology and Neurosurgery

1377. **Conditioning Techniques in the Treatment of Writer's Cramp**
L. A. Liversedge and J. D. Sylvester. *Lancet* [*Lancet*] **1**, 1147–1149, June 4, 1955. 4 figs., 4 refs.

This paper from the University of Manchester describes the treatment by a "deconditioning" technique of 6 patients suffering from writer's cramp and one suffering from typist's cramp. The authors suggest that, whatever the origin of such occupational cramps, their persistence may be due to the operation of a conditioned reflex. They have therefore devised ingenious but simple apparatus whereby a sensory counter-stimulus (electric shock) is applied whenever the tremor or spasm characteristic of the disorder becomes manifest.

The effect of daily treatment for 3 to 5 weeks on these 7 patients, most of whom had been affected for many years and had not benefited from drugs or psychotherapy, was distinctly promising. The degree of improvement bore no relation to mental and emotional constitution, in which the patients differed widely, and it is suggested that this lends support to the authors' view of the physiological mechanism underlying writer's cramp.

J. B. Stanton

1378. **A Critical Study of Kirschner's Technique of Coagulation of the Gasserian Ganglion in Trigeminal Neuralgia.** (Étude critique du procédé de Kirschner pour la coagulation du ganglion de Gasser dans la névralgie essentielle du trijumeau)
A. Dereymaeker, J. Dieu, and J. Spitaels. *Acta neurologica et psychiatrica Belgica* [*Acta neurol. psychiat. belg.*] **54**, 890–901, Nov., 1954. 7 figs.

In spite of their popularity with neurosurgeons the classic methods of retro-Gasserian neurotomy for the treatment of trigeminal neuralgia carry quite definite risks. In the authors' experience the indirect methods, such as that of Kirschner in which a simple stereotaxic instrument is used to simplify location of the foramen ovale, still have considerable value. This method has certain disadvantages of imprecision, however, and the present authors have improved its accuracy by confirming the positioning by a radiograph of the base of the skull, and have also minimized the tendency of the stereotaxic apparatus to slip by the introduction of a simple modification. The destruction of the trigeminal ganglion is then carried out by electrocoagulation.

In spite of these precautions it is not always possible to limit the procedure to the affected division of the nerve, and in some patients the ophthalmic division may be inadvertently destroyed. The resulting keratitis which follows this complication necessitated tarsorrhaphy in 5 of the 28 patients included in the study here reported from the Institute of Neurology, Louvain. On the whole, however, the results were considered satisfactory, recurrence being observed in only 2 cases, both of which were cured by a second coagulation; 5 patients were not benefited and one died under thiopentone anaesthesia.

Donald McDonald

1379. **A Case of Hodgkin's Disease of the Spinal Cord.** (Наблюдение лимфогрануломатоза спинного мозга)
V. V. Morozov. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] **19**, 56–57, May–June, 1955. 2 refs.

The author describes the case of a young male patient aged 23 who complained of pain in the legs and between the shoulders, which was shortly followed by weakness in the legs and pelvic disturbances. He became paraplegic a year later and areas of tenderness were found over the 4th and 5th thoracic vertebrae. The lymph nodes were not enlarged. Radiological examination showed many small foci of destruction in the body of the 4th thoracic vertebra. The haemoglobin value was 72% and the leucocyte count 10,000 per c.mm. Examination of the cerebrospinal fluid showed 46 cells per c.mm., of which 16% were neutrophil granulocytes and 84% lymphocytes. The Pandi reaction was positive. Compression of the jugular veins did not raise the pressure of the cerebrospinal fluid.

On laminectomy dense adhesions were found between the dura and the underlying tissue. Histological examination of the biopsy material showed features typical of Hodgkin's disease. The patient responded well to *x*-ray therapy and to "embikhin", but suffered a slight paralysis a year later, when the present report was written. The medullary lesion was probably a secondary manifestation but, apart from the vertebral involvement, no other lesions of Hodgkin's disease were found.

L. Crome

1380. **Electrocardiographic Patterns in the Differential Diagnosis of Progressive Muscular Dystrophy**
J. Schott, M. Jacobi, and M. A. Wald. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 517–524, May, 1955. 10 figs., 19 refs.

A chance observation some years ago that the amplitude of the QRS complex in some of the precordial leads of the electrocardiogram was often strikingly increased in patients suffering from the pseudohypertrophic type of progressive muscular dystrophy led to a study of the electrocardiographic features of 9 cases of the disease at the Jewish Chronic Disease Hospital, Brooklyn, New York, of which 6 were of the pseudohypertrophic type. Of these 6, the QRS complex in 4 was of a voltage greater than the accepted maximum in at least one precordial lead, and in the other 2 it was just within the maximum normal limit. In the 3 cases of the facio-scapulo-humeral type the potential of the QRS complex was of normal mean value. The tracings in each case are reproduced.

It is suggested that this finding is sufficiently constant to be of value in the differential diagnosis of muscular dystrophies.

Donald McDonald

1381. **Bilateral Lumbar Plexus Lesions Simulating Cauda-equina Compression**
A. R. TAYLOR and N. M. DOTT. *Lancet* [*Lancet*] **1**, 688–691, April 2, 1955. 3 figs., 4 refs.

The authors discuss the differential diagnosis of bilateral neurological involvement of the lumbar and/or sacral nerve roots due to increase in pressure within the psoas compartment from that due to intraspinal involvement of the cauda equina, with particular reference to the cases of 4 patients admitted to Edinburgh Royal Infirmary suffering primarily from inflammatory disease of the vertebral bodies, in which the pathological process had spread laterally and damaged the lumbar plexus on both sides. Detailed case histories are given.

The authors state that the diagnostic differentiation of the two conditions should not be difficult, provided that the possibility of the occurrence of the former is borne in mind. Whereas compression of the cauda equina almost always involves the sacral roots and causes bladder dysfunction, in lesions of the plexus the neural involvement is usually asymmetrical and bladder function is normal. Also in the latter the primary focus of disease, often tuberculous, in the vertebral bodies causes radiological changes, and radiography may reveal the presence of a psoas abscess. The authors suggest that compression of the vasa nervorum of the lumbar plexus is the primary cause of the nerve changes, and that this can best be relieved by closed or open drainage of the psoas compartment, the anatomy of which is briefly discussed. *Donald McDonald*

BRAIN AND MENINGES

1382. **The Etiology of Cerebral Palsy**
N. J. EASTMAN and M. DELEON. *American Journal of Obstetrics and Gynecology* [*Amer. J. Obstet. Gynec.*] **69**, 950–961, May, 1955. 5 refs.

In an attempt to determine the obstetrical factors involved in the aetiology of cerebral palsy, the antenatal, obstetrical, and postnatal histories of 96 affected infants born at the Johns Hopkins Hospital, Baltimore, between 1945 and 1949, are compared with those of 11,195 normal infants born during the same period. Such factors as the mother's age, parity, and type of pelvis did not appear to be related to the development of cerebral palsy in the child, and the same applied to toxaemia, virus infections during pregnancy, and the total duration of labour. The incidence of Rh-negative women among the mothers of the 96 affected children was no higher than in the general population, and in fact none of the children had erythroblastosis foetalis. Postmaturity and prolapse of the cord were also shown to bear no relationship. It was not possible to relate any type of neurological disability to any particular obstetrical complication. However, nearly half the infants who later proved to have cerebral palsy were obviously in poor condition immediately after birth compared with only 2% of the controls.

Although breech delivery was twice, and mid-forceps delivery three times, as frequent in the series with cerebral palsy as in the control series, the authors consider that the aetiological importance of mechanical injury at birth has been overestimated, since the proportion of such cases was small in both groups. Again, a second stage of labour of more than 3 hours was more common in the former series, though relatively uncommon in both, but in any case it is difficult to say whether the deleterious effect of a prolonged second stage is due to injury or to anoxia. While there was a fairly high incidence of malformations of all kinds and degrees among the cases of cerebral palsy (14·6% as opposed to 3·8% in the controls), suggesting that genetic factors or infective processes early in pregnancy may have been important in a certain proportion of cases, prematurity and foetal anoxia appeared to be of much more significance. The incidence of prematurity was 35·4% among the infants developing cerebral palsy, compared with an over-all incidence of 9·2%, and the degree of prematurity was closely related to the likelihood of cerebral palsy. In only 11 out of the 34 premature births among the affected children was there severe anoxia caused by placenta praevia or abruptio placentae, and the authors are of the opinion that prematurity *per se* is causally related to cerebral palsy. Nevertheless, there was considerable evidence that placental separation, with subsequent partial anoxia, is also an important factor; thus while the frequency of bleeding before the 20th week of pregnancy was the same in the two series, bleeding after the 20th week was five times more common in the series with cerebral palsy.

Intrapartum fever was present in 9·4% of the mothers of infants developing cerebral palsy and in only 1·3% of the controls, while prolonged postnatal fever occurred in 30·2% of the former babies, but in only 0·1% of the controls: it is pointed out, however, that intrapartum fever is most likely to develop in prolonged labours, often calling for forceps delivery, and would raise the oxygen requirement of the infant's brain, while postnatal fever may well have been due to brain injury and would also have increased the cerebral oxygen requirement and contributed to anoxia. There is thus no need to regard infection as a direct cause of cerebral palsy in these cases.

From a general review of the data available it seems likely that in many cases a number of factors combined to act adversely upon the child. Thus in only 18 of the 96 cases were pregnancy and labour judged to have been "normal" in that they met the reasonable criteria laid down by the authors. *J. Foley*

1383. **Studies in Cerebrovascular Disease. IV. The Syndrome of Intermittent Insufficiency of the Carotid Arterial System**
C. H. MILLIKAN and R. G. SIEKERT. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **30**, 186–191, May 4, 1955. 9 refs.

The authors seek to emphasize the diagnostic importance of the intermittent premonitory symptoms which may precede thrombosis of the internal carotid artery. On the basis of their observations in 8 cases (which are described) they define the features of a syndrome which they suggest should be called "the syndrome of intermittent insufficiency of the internal carotid arterial system". It is characterized by attacks of unilateral

impairment of motor or sensory function or both, associated in certain instances with a disorder of speech or homolateral involvement of vision or both. It is claimed that sufficient arteriographic, surgical, and pathological evidence is now available to confirm that attacks of this kind are related to disease of the internal carotid artery. Differential diagnosis from intracranial space-occupying lesions may sometimes be difficult, but the latter are generally excluded by the remittent nature of the symptoms. Differentiation from the syndrome of intermittent basilar insufficiency may also be difficult in cases in which there is little else except evidence of unilateral impairment of motor or sensory function. However, when the carotid artery is involved there is a palpable diminution in pulsation in that artery or a unilateral decrease in retinal blood pressure; signs of bilateral involvement or of dysfunction of cranial nerve nuclei will point to disease in the basilar artery. The authors are unable to say whether total occlusion of the artery invariably develops in patients with this syndrome, nor do they produce evidence to explain the pathogenesis of the intermittent attacks. They advise, however, that patients with this syndrome should be treated with anti-coagulant drugs, unless there is some contraindication to such treatment. *John N. Walton*

1384. **The Use of Hypothermia in Surgical Treatment of Cerebral Vascular Lesions. A Preliminary Report**
W. M. LOUGHEED, W. H. SWEET, J. C. WHITE, and W. R. BREWSTER. *Journal of Neurosurgery* [*J. Neurosurg.*] **12**, 240–255, May, 1955. 10 figs., 3 refs.

1385. **Evaluation of Carbon Dioxide Inhalation for Acute Focal Cerebral Infarction**
C. H. MILLIKAN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **73**, 324–328, March, 1955. 18 refs.

At the Mayo Clinic the author has studied the effects of the inhalation of 5% carbon dioxide in oxygen on patients with recent cerebral infarction. Since carbon dioxide produces cerebral vasodilatation during the inhalation period it was thought this might be a useful method of reducing the amount of brain damage and of promoting recovery of the damaged area. The author is careful to point out, however, that in a condition running such a variable course as cerebral infarction the benefit of any particular treatment is difficult to assess. Also, the pathological physiology of cerebral infarction is so poorly understood that it is not known whether an increase in cerebral blood flow is desirable, or whether there may not even already be maximal vasodilatation before treatment owing to local accumulation of carbon dioxide in the anoxic brain tissue.

To the author's series of 50 patients with acute focal cerebral infarction the gas mixture was administered for 5 to 12 minutes hourly for the first 48 hours, and then hourly during the day only for a further 5 days. At the end of 14 days the results were compared with those in 225 similar cases not so treated. On the whole they were slightly more favourable in the treated group; but it is suggested that more work must be done on this particular line of treatment before its value can be fully evaluated. *G. S. Crockett*

1386. **Benign Postinfectious Disorder of Anterior Midbrain. Alternating Contraction Anisocoria, Combined with General Fatigue and Peripheral Neuritis**
O. LOWENSTEIN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **73**, 302–308, March, 1955. 6 figs., 4 refs.

From the Institute of Ophthalmology, Presbyterian Hospital, New York, the author describes a syndrome seen in a proportion of patients recovering from virus encephalomyelitis, of which the main component is a pupillary reaction, alternating contraction anisocoria, which, he suggests, indicates a lesion in the anterior part of the midbrain. (This sign was fully described in a previous communication by the author (*Arch. Neurol. Psychiat.* (*Chicago*), 1954, **72**, 742; *Abstracts of World Medicine*, 1955, **18**, 68).) He considers that when this sign is combined with prostration, excessive general fatigue and increased fatiguability, mental depression, and peripheral neuritis, it indicates a benign "sub-chronic" encephalomyelitis of virus origin, which may take from 6 months to 2 years to clear up entirely. Three such cases are described in detail and 19 others are cited, all of which occurred in patients recovering from an acute attack of virus infection. *G. S. Crockett*

1387. **Parsidol in the Treatment of Parkinsonism**
D. K. ZIEGLER and F. TORRES. *Neurology* [*Neurology*] **5**, 197–200, March, 1955. 6 refs.

The synthetic drug diethylamino-2-propyl-1-N-phenothiazine ("parsidol"; "lysivane") was given alternately with a placebo to 30 patients with Parkinsonism at the Veterans Administration Center, Los Angeles. Of these, 3 reported an improvement with the placebo and 10 complained that it had an adverse effect, and were therefore not considered reliable. Of the remaining 17, 13 reported a reduction in the rigidity and tremor, and in 10 of these neurological examination provided some objective confirmation of this improvement. The optimum dose was found to range from 200 to 400 mg. a day, a dosage considerably larger than that used by previous workers. However, no haematological complications were observed. The drug is compatible with solanaceous drugs, "artane" (benzhexol hydrochloride), and antihistamines and indeed appeared to show some synergism with them. *Donald McDonald*

1388. **Kemadrin in the Treatment of Parkinsonism**
R. S. SCHWAB and M. E. CHAFETZ. *Neurology* [*Neurology*] **5**, 273–277, April, 1955. 5 refs.

The value of "kemadrin" (procyclidine) was compared with that of "artane" (benzhexol hydrochloride) and "pagitane" in the treatment of 87 patients at the Massachusetts General Hospital, Boston, suffering from postencephalitic and other forms of Parkinsonism. A number of objective tests, previously described by Schwab *et al.*, (*Arch. Neurol. Psychiat., Chicago*, 1951, **65**, 489; *Abstracts of World Medicine*, 1951, **10**, 425) were carried out in each case, the findings being supplemented by the

patient's subjective evaluation of the treatment and a neurological assessment of the results. Of the 87 patients, 38 were considerably improved, 12 by kemadrin alone and 26 by kemadrin with " thephorin " (phenindamine hydrogen tartrate) or diphenhydramine hydrochloride.

The authors, while emphasizing the difficulty of assessing the effect of any particular drug in the treatment of Parkinsonism, conclude from their findings that kemadrin is as effective as artane or pagitane and is another useful drug in the treatment of this condition.

J. B. Stanton

1389. **" Largactil " (" 4560 R.P.") in the Treatment of Hypertonic and Dyskinetic Syndromes.** (Il largactil (4560 R.P.) nelle sindromi ipertoniche e discinetiche)
E. MANGHI. *Giornale di psichiatria e di neuropatologia* [*G. Psichiat. Neuropat.*] **82**, 959–969, 1954. 16 refs.

A considerable part of this paper from the University of Parma is devoted to a review of the various drugs that have been introduced for the treatment of Parkinsonism. Because of its reported relaxant action " largactil " (chlorpromazine) was given to 10 patients suffering from this disease, but with very little success; there was a certain reduction in muscular tone, but this was almost invariably accompanied by severe muscular weakness, and in some cases led to a condition closely resembling coma vigilans.

The drug was also administered in 15 cases manifesting hyperkinetic syndromes, all of a choreiform nature. In this type of disorder the depressant action of chlorpromazine was found to be beneficial. But in a further trial of the drug on 7 patients suffering from hypertonic paralysis due to upper motor neurone lesions of the pyramidal tract the only apparent effect was that the hypertonus was reduced [but not, it would appear, by any very useful degree]. *Donald McDonald*

EPILEPSY

1390. **Effects of Photic Stimulation during Sleep. A Study of Normal Subjects and Epileptic Patients**
E. A. RODIN, D. D. DALY, and R. G. BICKFORD. *Neurology* [*Neurology*] **5**, 149–159, March, 1955. 4 figs., 16 refs.

It is now well known that the flashing of a light in a subecjt's eyes causes waves of a corresponding rhythm to appear in the electroencephalogram (EEG) obtained from the occipital cortex, and that in susceptible subjects this may be accompanied by epileptiform seizures. In the present investigation, carried out at the Mayo Clinic, 5 normal subjects and 76 epileptic patients were investigated during natural sleep or sleep induced by sedatives, photic stimulation being given by a stimulator producing brief flashes 50 microseconds in duration at various frequencies from 1 to 30 per second and an intensity of 250,000 foot-candles (approximately 2,700,000 lumens per sq. metre). With this degree of intensity the stimulus was as effective, in the waking condition, with the eyes open as with the eyes closed, and it is thought that it is transmitted through the sclera. A constant distance of 15 cm. was maintained between the subject's eyes and the light source.

In the normal subjects flashes at the rate of 20 per second elicited the same response during sleep as when awake, but the intensity of the response at this frequency was reduced, and apparently diminished progressively in proportion to the depth of sleep. In the first group, of 30 epileptic patients known to be subject to convulsions as a result of light stimulation, the results during sleep were of the same kind as in the normal subjects, namely, a markedly reduced response. Mild seizures were observed in only 4 patients and 13 showed no EEG response. The greater relative reduction of activity in these patients was attributed to the fact that most of them had received sedatives, and so sleep was probably deeper than in the normal subjects.

In the second group. of 46 epileptic patients who were not sensitive to light the results were essentially the same as in the normal subjects.

The results of this investigation raise interesting questions as to the role of reduced afferent stimulation of the cerebral cortex as a cause of sleep, since it would appear that a standard stimulus reaches the cortex with less intensity during sleep. In the case of the optic pathway the authors consider this diminution to occur at the lateral geniculate body [but this is only a speculation with little supporting evidence as yet].

Donald McDonald

1391. **Respiratory Changes in Epileptic Seizures.** (Modifications respiratoires dans les paroxysmes épileptiques)
H. FISCHGOLD and —. ARFEL-CAPDEVIELLE. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **7**, 165–178, May, 1955. 7 figs., 20 refs.

In major epilepsy apnoea, which appears to be due to respiratory and laryngeal spasm, is a constant feature of the attack and the resultant anoxia is generally regarded as a factor in the termination of the tonic phase. Respiratory changes during minor attacks too have been observed by the authors at the Hôpital Sainte-Anne, Paris, in 7 subjects with petit-mal " absences " and in 4 subjects with temporal-lobe attacks, the electroencephalogram also being recorded. In the former group respiratory arrest occurred in 10 out of 12 attacks involving loss of consciousness but in only one of 7 when the electrical changes were not accompanied by unconsciousness. On the other hand, despite marked emotional and vasomotor changes, the temporal-lobe attacks were not associated with any such clear respiratory changes.

In discussing the possible mechanisms by which respiration may be involved in petit-mal attacks the authors consider the brain-stem reticular system to be of prime importance for the initiation of attacks but, in view of the ease with which these attacks may be precipitated by biochemical and other stimuli, such as flicker, feel that the primary effect might be at a variety of levels. On the other hand direct involvement of

the limbic cortex in the local discharge might be sufficient to explain the lesser respiratory upset of the temporal-lobe attack. *William Cobb*

1392. **Desoxyn Therapy for Nocturnal Seizures. A Preliminary Report**
J. LOGOTHETIS. *Neurology* [*Neurology*] **5**, 236–241, April, 1955. 24 refs.

" Desoxyn " (methylamphetamine hydrochloride) was tried in the treatment of 46 patients suffering from convulsive disorders, the drug being given in addition to any other anticonvulsant therapy. It was well tolerated, only a few mild reactions being observed. Of 20 patients having nocturnal seizures, 13 were greatly improved, there being a reduction of at least 50% in the number of such seizures. Of 26 patients who had seizures in the daytime, only one with petit mal benefited from this treatment; indeed, in 13 of the patients the frequency of the seizures increased.

Discussing the results the author states that from experimental evidence it would appear that sleep provides a better background for precipitation of a seizure in the presence of a diencephalic focus than in the presence of a cortical focus. He suggests that desoxyn is effective in nocturnal and petit-mal seizures through its cortical stimulating action, producing an inhibition of seizure discharges from the diencephalon. *J. B. Stanton*

DISSEMINATED SCLEROSIS

1393. **Multiple Sclerosis and Amyotrophic Lateral Sclerosis. Etiological Significance of Recent Epidemiologic and Genetic Studies**
L. T. KURLAND, D. W. MULDER, and K. B. WESTLUND. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 649–653 and 697–702, April 21 and 28, 1955. 2 figs., bibliography.

Recent epidemiologic and genetic data in association with clinical and pathological observations are compared for multiple sclerosis and amyotrophic lateral sclerosis. The most striking epidemiologic characteristic for multiple sclerosis is its rarity in the tropics and subtropics and its relatively high prevalence in regions with a " colder " climate. No selectivity for race or nationality within any particular area was observed. The importance of a genetic factor in multiple sclerosis is equivocal, and the data strongly suggest that an exogenous factor is of prime importance.

On the other hand the geographic distribution of amyotrophic lateral sclerosis does not vary in the countries and regions studied except for the Mariana Islands, where this illness is exceedingly prevalent. No external etiologic factor has been discovered on Guam in the Mariana Islands or elsewhere, but the occurrence of numerous cases in some families and none in neighbouring families was noted. In a recent genetic study of amyotrophic lateral sclerosis, a large number of pedigrees indicative of dominant inheritance were collected. It is uncertain whether the " sporadic " cases of amyotrophic lateral sclerosis that still account for the majority of all cases observed in practice have a basic etiology differing from that of the hereditary form of the disease. The data strongly suggest that for amyotrophic lateral sclerosis exogenous factors are of little importance etiologically; it is inferred that this disorder is due to some yet undetected metabolic disturbance that develops in adulthood and is often inherited.—[Authors' summary.]

1394. **Blood Platelets in Disseminated Sclerosis. Quantitative Variations in Peripheral Blood**
T. FOG, I. KRISTENSEN, and H. F. HELWEG-LARSEN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **73**, 267–285, March, 1955. 17 figs., 19 refs.

The variations in the platelet count were observed in 10 healthy subjects and in 103 cases of inactive disseminated sclerosis, 11 active cases, and 30 cases of other neurological disorders in patients attending the Neurological Clinic, Rigshospitalet, Copenhagen. The counts were performed on peripheral blood daily (except Sundays), in most cases for one month.

The counts showed greater variation in the number of platelets in patients with active or inactive disseminated sclerosis than in the other two groups of subjects, the fluctuations being greatest in those with active disease. There was a fall in the platelet count of between 200,000 and 500,000 per c.mm. of plasma during phases of activity of the disease; a similar fall has been noted during the course of any infective disease. The fluctuation in these cases, however, is interesting in view of the finding of " clots " of blood platelets in the central veins of fresh foci of neurological damage in this disease. (The paper is accompanied by numerous charts and several case histories.) *G. S. Crockett*

1395. **Visual and Motor Instability in Multiple Sclerosis**
J. EDMUND and T. FOG. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **73**, 316–323, March, 1955. 11 refs.

A study of the records of 152 cases of disseminated sclerosis admitted to the Neurological Clinic of the City Hospital, Copenhagen, showed that 44 (28%) complained of a deterioration of their condition when under stress. The authors have therefore studied in detail the deterioration in visual acuity and other neurological changes in patients with disseminated sclerosis when subjected to stress in the form of exposure to heat.

When 41 patients were heated in a hot air bath to 55 to 60° C. for 20 minutes 32 of them showed a positive reaction to heating, that is, their visual acuity deteriorated or motor signs and symptoms were aggravated. The effect was most marked in those in whom the disease appeared to be active and in those most severely affected by it. The deterioration was generally observed to begin some 10 to 15 minutes after heating and lasted for 15 minutes. (The authors also made the interesting discovery that myopia is commoner in Denmark among patients with disseminated sclerosis than among the general population.) They consider that the visual impairment is possibly due to oedema of the posterior capsule of the lens. *G. S. Crockett*

Psychiatry

1396. **Frequency and Types of Mental Retardation in Twins**

G. ALLEN and F. J. KALLMANN. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] 7, 15–20, March, 1955 [received May, 1955]. 9 refs.

This is a preliminary report on a study of mentally retarded twins and deals largely with general statistical data. At the time of analysis, the series included 601 index cases representing 478 multiple births. The earliest admission was in the year 1907, and ascertainment is almost complete for recent admission years (1954 and thereafter).

In the institutional population studied, twins were found to constitute 3·1% of all admissions, as compared with about 2% of twins expected in the general population of the State of New York. The observed excess of twins occurs in all major diagnostic categories and seems to be only partly explained by factors related to twinning *per se*. In every major diagnostic category listed, concordance with respect to certified mental deficiency is more frequent in same-sex than in opposite-sex twin pairs. For some categories concordance is found only in same-sex pairs. More detailed studies are in progress.—[Authors' summary.]

1397. **Incidence, Mortality, and Sex Distribution of Mongoloid Defectives**

R. G. RECORD and A. SMITH. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] 9, 10–15, Jan., 1955. 14 refs.

An attempt was made to trace all cases of mongolism among children born during the 11 years 1942–52 in Birmingham. From the records of hospitals and the Public Health Department 252 mongols were identified among a total of 231,619 births (1·09 per 1,000). The incidence of mongolism appeared to be higher among children born in hospital than among those born at home or in nursing homes, but this may have been due to incomplete diagnosis in the latter groups. It is estimated that nearly two-fifths of those mongols who were alive shortly before birth were dead at the end of the first montn, less than half survived the first year, and only about two-fifths were alive at 5 years. Death was most commonly due to respiratory infections, but in some cases it was the result of gastro-intestinal infections or congenital malformations.

The mortality in infancy was greater for females than for males, and it is suggested that this accounts for the inverse correlation between the sex ratio (percentage of males) and maternal age reported by Kieg (*Ann. paediat. (Basel)*, 1951, **177**, 31), since infant mortality has been shown to rise with maternal age. It also explains the inverse correlation to be found between the recorded incidence of the condition in a series and the sex ratio of its members. *Kathleen M. Lawther*

1398. **Maternal Age and Birth Rank in the Aetiology of Mongolism**

A. SMITH and R. G. RECORD. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] 9, 51–55, Jan., 1955. 21 refs.

The incidence of mongolism in relation to maternal age and birth rank was studied at the University of Birmingham by comparing data for 217 mongoloid infants born in Birmingham between 1942 and 1952 with those from a control series of 1,156 infants representative of all births in the city during the same period. The incidence of mongolism showed the usual well-marked increase with maternal age, and this trend was shown to be little affected by eliminating the influence of birth rank. The apparent increasing incidence of mongolism with birth rank was largely eliminated when the influence of maternal age was removed, the incidence then being greater in first-born than in later born infants at all maternal ages below 40. *Kathleen M. Lawther*

1399. **The Association of Dementia with Radiologically Demonstrated Cerebral Atrophy**

R. H. GOSLING. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] 18, 129–133, May, 1955. 1 fig., 10 refs.

The case notes of all patients with dementia of onset after the age of 45 who had been subjected to examination by air encephalography at the National Hospital, Queen Square, London, over a 4-year period were studied, cases of degenerative disease with systemic involvement of the central nervous system, trauma, cerebral tumour, and cerebrovascular disease in which the neuropathology was beyond dispute being excluded. This left 68 cases, in 58 (85%) of which cerebral atrophy was radiologically demonstrable. Of the 10 remaining patients, 6 were traced one year later and of these only one showed progressive deterioration; moreover, rescrutiny of the films showed that in only one case could abnormality definitely be excluded. Of 213 patients without clinical evidence of dementia who were subjected to air encephalography during the same period, radiological signs of cerebral atrophy for which no cause could be found occurred in 24, most of them cases of " epilepsy of late onset ".

The encephalograms from these 24 cases were then compared with those from 39 of the 58 demented patients, those with only slight dementia being omitted. The features in the encephalogram that were found to be of value in distinguishing cases of cerebral atrophy with associated dementia from those without were: (1) cortical sulci of width greater than 0·5 cm.; (2) presence of air trapped in the insular region of the cortex; (3) enlargement of one or both lateral ventricles particularly marked in the region of the trigone, whether or not they were enlarged elsewhere. By these criteria the presence or

absence of dementia could be predicted in about 3 cases out of 4.

[This is an interesting and thoughtful paper, which clearly demonstrates the potential value of air encephalography in cases of dementia in late middle life. It suffers, however, from the defects inherent in any retrospective investigation of a population selected through the medium of hospital case records. As indicated by the author, there are reasons to doubt whether the findings are valid for all types of dementia of later life, and a good case is made for testing the validity of these preliminary findings on a larger population, including patients admitted to mental hospitals, and with stricter criteria for the diagnosis of dementia, more precise methods of interpreting the encephalograms, and a long-term follow-up.] *J. A. Harrington*

TREATMENT

1400. Orbital Leucotomy. A Review of 52 Cases
G. C. KNIGHT and R. F. TREDGOLD. *Lancet* [*Lancet*] **1**, 981–986, May 14, 1955. 4 figs., 18 refs.

Orbital leucotomy was introduced into Great Britain in 1949, and since 1951 more than 50 cases of neurotic tension have been subjected to this procedure at the Brook Hospital, Blackheath. In this paper are reported the results of an analysis of the psychological condition of 52 patients so treated. The criteria for selection of patients for this operation have not been rigidly defined, but most of them had severe anxiety or depression which caused much misery to themselves and their relatives and which had not been relieved by other methods.

After a brief review of the surgical treatment of mental disorder, an account is given of the operation, which consists in undercutting the orbital cortex of the frontal lobe from the frontal pole to the level of the tip of the ventricle, along a plane parallel with the orbital plate, the incision avoiding the lateral aspect of the lobe.

Of the 52 patients, 23 were "markedly improved", 21 had "some improvement", and 7 were unchanged; deterioration of personality was recorded in only one case. Age and previous response to electric convulsion therapy appeared to have no prognostic value, but cases with hysterical symptoms seemed unsuitable for the operation. Some patients derived benefit from psychotherapy after the operation, even when such treatment had been of no avail before. *J. B. Stanton*

1401. Undercutting of Orbital Cortex in Chronic Neurotic and Psychotic Tension States
R. STRÖM-OLSEN and D. W. C. NORTHFIELD. *Lancet* [*Lancet*] **1**, 986–991, May 14, 1955. 6 figs., 8 refs.

In this paper from Runwell Hospital, Wickford, Essex, are presented the results of bilateral undercutting of the orbital cortex in 27 psychiatric patients. These included both those with well-preserved personalities (13) and those who had deteriorated (14), and both chronic neurotics (7) and chronic psychotics (20). The operation is described and illustrative case histories are included, together with the neuro-anatomical findings in 2 patients who died 5½ months and 2½ years respectively after the operation. In general terms the results were as follows: recovered, 8; improved, 13; not improved, 5 (including the 2 fatal cases); unchanged, 1.

In view of these good results and the absence of serious postoperative personality defects and other complications, the authors suggest that undercutting of the orbital cortex is preferable to standard leucotomy in cases of intractable chronic neurosis and depression, and in well-preserved psychotic patients in whom tension and psychomotor unrest are marked. *J. B. Stanton*

1402. Use of Dehydroisoandrosterone in Psychiatric Practice
E. B. STRAUSS and W. A. H. STEVENSON. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 137–144, May, 1955. 1 fig., 5 refs.

A preliminary clinical study of the therapeutic effects of dehydro*iso*androsterone was made at St. Bartholomew's Hospital, London, on 11 selected male patients whose ages ranged from 14 to 46. While the patients exhibited a widely varying symptomatology, all were characterized by "constitutional immaturity", and showed evidence of being "inadequate but not psychotic".

Where possible, the 17-ketosteroid output and the blood count were determined and a Rorschach test was carried out before and after treatment. The dosage varied, ranging from 2·5 to 25 mg. daily in several doses, and the period of treatment was similarly variable. Some response to the drug was noted in all cases, the patients reporting increased confidence, energy, interest, and ability to deal with their personal problems, and the observers reporting less apathy and more virility and drive. In 3 cases the improvement was dramatic and lasted up to a week after discontinuing the drug. In some cases the leucocyte count showed a change in the ratio of lymphocytes to granulocytes, but there was no significant fall in the total count during treatment. No significant correlation between the mental improvement and 17-ketosteroid excretion was found. Symptoms of overdosage included restless activity, euphoria, mild hypomania, and increased aggressiveness. Contra-indications to treatment are antisocial behaviour and marked aggressiveness. From the results of the test on these patients it would appear that cases showing "ambiequality" are those most likely to be improved by the drug.

[Whether or not dehydro*iso*androsterone will prove to be of lasting value in psychiatry awaits a scientifically controlled study—only 2 of the authors' patients were given dummy tablets for a week for control purposes, while the issue in some cases was confused by the concomitant application of additional drugs and therapies. The terms "immaturity" and "inadequate" are not given an operational definition, and are doubtfully valid concepts. However, the findings reported do indicate that dehydro*iso*androsterone may produce an alteration in mental state: the precise nature of that change, if any, awaits further elucidation.] *J. A. Harrington*

1403. **An Appraisal of Histamine Therapy in Schizophrenia**

Y. ROULEAU, G. NADEAU, J. DELÂGE, M. COULOMBE, and M. BOUCHARD. *Journal of Clinical and Experimental Psychopathology* [*J. clin. exp. Psychopath.*] **16**, 1–9, Jan.–March, 1955. 1 fig., 22 refs.

At the Hôpital Saint-Michel-Archange, Quebec, histamine was tried in the treatment of 100 schizophrenic patients (80 males and 20 females) aged 14 to 48 years. A subcutaneous injection of 0·25 to 0·5 mg. of histamine base (0·75 to 1·50 mg. of histamine phosphate) was given initially and repeated 45 minutes later; this dosage was increased daily until definite symptoms of intolerance were observed, treatment being continued for 30 days. The mean dosage for the group was 9·3 mg. of histamine base, but some patients tolerated two 20-mg. doses while in a few psychoneurotics there were toxic reactions with doses as small as 3 mg. of histamine base.

In 20 cases the improvement was such that the patient could be discharged from hospital, 5 of them losing their hallucinations. The duration of the illness in 14 of these 20 patients was less than 18 months. Of the remaining 80 patients, 76 were then given electric convulsion therapy (E.C.T.) alone (20 treatments each); only one showed any significant improvement. Of 4 given thyroid extract with E.C.T., 3 were benefited, and of 11 given insulin shock treatment after E.C.T., only 2 were improved. *G. de M. Rudolf*

1404. **Reserpine ("Serpasil") in the Management of the Mentally Ill**

R. H. NOCE, D. B. WILLIAMS, and W. RAPAPORT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 11–15, May 7, 1955. 1 ref.

Reserpine was given for periods up to 12 months to 247 mentally-ill patients (30 males and 217 females) at Modesto State Hospital, Modesto, California. The ages of the patients ranged from 15 to 80 years (average 44 years) and all except 15 were psychotic, mostly schizophrenic. The drug was given intravenously or intramuscularly daily or on alternate days for 5 to 10 days. The dosage [not clearly stated] seems to have varied from 2·5 to 10 mg.; for the first week 1 mg. was also given by mouth twice a day. After this, the dosage was determined by the amount needed to produce maximum therapeutic response with minimum psychomotor retardation, and needed constant adjustment. In elderly patients with severe arteriosclerosis only half the dosage was given, in order to prevent syncope or hypotensive episodes. The authors emphasize that adequate dosage of reserpine over a long period may produce more satisfactory results than smaller doses over a short period. Side-effects, which were minimal and inconstant, included flushing, nausea, thirst, polyuria, and diarrhoea. Hypotension and bradycardia occurred in a few cases, but these were asymptomatic and responded to ephedrine sulphate.

Electric convulsion therapy (E.C.T.) was given to 56 patients in addition to reserpine; in some of these, especially patients whose mental condition had deteriorated, there was more improvement than with E.C.T. or reserpine given alone, while many improved to the point where E.C.T. could be discontinued, or, owing to the potentiating effect of reserpine, the number of treatments could be reduced. It was noted that the convulsive threshold was lowered by reserpine. Only a few of the patients given barbiturates in addition to reserpine improved, most of them becoming worse until barbiturates were withdrawn. Reserpine proved efficacious in many agitated senile and arteriosclerotic patients whose condition had not responded to barbiturates.

Of the total number of patients, 36% were markedly improved, 28% moderately improved, and 20% slightly improved; there was no improvement in 15%. [Patients considered to be markedly improved might have been in remission.] Altogether 27·9% left the hospital on discharge or indefinite leave of absence, including many whose condition had previously been regarded as hopeless. The authors state that in 85% nursing care was facilitated by this treatment, the patients being less untidy and destructive and more sociable and cooperative. Insight was often better, resulting in a will to improve, and the number of psychiatric interviews necessary decreased. In many cases appetite increased, 75% of the patients gaining significantly in weight, and constipation was alleviated. The best response was observed in the paranoid and catatonic types of case, 30% and 45% respectively being markedly improved.

The authors conclude that reserpine should be tried in both neurotic and psychotic patients before more radical treatment is carried out. *Elizabeth M. Watkins*

1405. **Treatment of Two Hundred Disturbed Psychotics with Reserpine**

J. A. BARSA and N. S. KLINE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 110–113, May 14, 1955, 7 refs.

Reserpine in a fairly high dosage was given to 200 severely disturbed psychotic patients, all females, for 3 to 9 months. During the first 10 days 3 mg. was given by mouth and 5 mg. by intramuscular injection each morning. If there was a beneficial response the intramuscular dosage was gradually reduced; if there was no sign of improvement the dose by injection was slowly increased to 10 mg. daily for 5 days and if there was still no improvement the injections were gradually discontinued. All the patients continued throughout to receive 3 mg. of reserpine by mouth daily, this being the optimum maintenance dose for most of them.

Three stages in the patient's response were recognized: an initial sedative stage beginning soon after the drug was first administered and lasting 3 to 10 days; a turbulent stage lasting one day to 3 weeks; and, in the successfully-treated patient, an integrative stage. Side-effects, such as drowsiness, mental confusion, tremor, epileptic seizures, or Parkinsonism, disappeared when the dose of reserpine was reduced.

Of the 200 patients, 120 were markedly or moderately improved, 32 being well enough to be discharged. The authors state that since the introduction of reserpine electric convulsion therapy has not been necessary in their clinic, although previously 150 such treatments were given each week. *F. K. Taylor*

Dermatology

1406. **Silicon Granuloma of the Skin**
P. M. CROSSLAND. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **71**, 457–461, April, 1955. 2 figs., 23 refs.

Traumatic silicon granuloma, which may follow injury of the skin with sand, soil, flint, slate, gravel, glass, cement, brick, or coal, often presents a difficult diagnostic problem. The lesion may not appear for many years (up to 45 years has been reported) after the injury. The history may reveal that there was delayed healing of the initial wound. Clinically there may be erythematous papules or nodular dermal lesions and microscopically there is tubercle formation (without caseation), consisting of epithelioid and Langhans giant cells but only a few lymphocytes. Anisotropic crystalline material may be seen lying free or within giant cells. Examination under polarized light should be carried out, but it is pointed out that cholesterol, cholesterol esters and the lipids found in xanthomata, histiocytes, and foreign body granulomata are also doubly refractive and cannot be distinguished by this means from silicon. *X*-ray absorption spectrography, which is the surest method of diagnosing these lesions, is, however, rarely available.

In the differential diagnosis sarcoidosis, tuberculosis cutis, and other granulomata must be considered. The tuberculin reaction may or may not be affected. The lesion in silicon granuloma is always strictly confined to the site of the original injury. A history of traumatic contact with broken fluorescent light bulbs may be significant. The author describes a case of silicon granuloma in a young married woman in whom the lesion appeared in scars on the knees 11 years after a fall on gravel. The lesions regressed spontaneously during the 6 months following their appearance, without treatment, leaving only a copper-coloured pigmentation.

S. T. Anning

1407. **A Contribution to the Internal Treatment of Benign Infectious Warts.** (Beitrag zur intern-medikamentösen Behandlung benigner infektiöser Epitheliosen)
W. HARTMANN. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **131**, 505–510, 1955. 21 refs.

At the City Hospital, Berlin–Spandau, 38 patients with common warts were treated by oral administration of the tinctures of *Thuja occidentalis* and *Artemisia abrotanum*, 10 drops of each in water being taken 3 times a day before meals. After 4 to 6 weeks of continuous treatment 25 of the patients (66%) were free of warts. This is considered to be significantly better than could be expected with placebos. The results were best in the youngest patients aged 5 to 10 years. Of 6 cases of verruca planus, the lesions were cleared in 5 after 2 to 7 weeks of this treatment. Of 9 patients with molluscum contagiosum, 6 appeared to respond to the treatment in 4 to 8 weeks. It is suggested that the mode of action may be through alteration of the peripheral circulation, but no experimental proof of this could be adduced. No untoward side-effects were noted.

[With the possible exception of molluscum contagiosum, the treatment of these types of wart by suggestion alone has given similar results, and therefore the present treatment may have worked through the same mechanism.] *G. W. Csonka*

1408. **A Valuation of Hydrocortisone Ointment**
B. RUSSELL, J. S. PEGUM, N. A. THORNE, and R. V. GRANGE. *Lancet* [*Lancet*] **1**, 1038–1043, May 21, 1955. 8 figs., 23 refs.

From the London Hospital a controlled trial is reported of an ointment consisting of 2·5% hydrocortisone acetate in polyethylene glycol in the treatment of 132 patients with various dermatoses. In alternate weeks the base alone was applied; in some cases the treatment began with the ointment and in some with the base, the patients being unaware that the preparations were different. Hydrocortisone ointment was found to be strikingly effective in lichen simplex, discoid eczema, otitis externa, and ano-genital pruritus. There was less obvious improvement in cases of cryptogenic eczematous dermatitis of the hands and of infantile eczema. In Besnier's prurigo there was sometimes local improvement, but on the whole the results were poor. One patient was sensitive to the vehicle (but obtained relief from hydrocortisone in hydrous ointment) and one complained that the ointment caused a burning sensation. In one case the infection increased during treatment.

The authors state that they have obtained good results with hydrocortisone ointment in contact dermatitis (not included in the controlled trial). *E. Lipman Cohen*

1409. **Hypothyroid Pruritus. (On the Etiology and Treatment of Certain Cases of Neurotic Excoriations.)** [In English]
S. GOLDBLATT. *Acta dermato-venereologica* [*Acta derm.-venereol. (Stockh.)*] **35**, 167–173, 1955. 2 refs.

1410. **Hydrocortisone Therapy in Control of Anogenital Pruritus. Preliminary Report**
R. TURELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 173–175, May 21, 1955. 9 refs.

In reporting the results of topical application of hydrocortisone acetate in ano-genital pruritus the author groups his cases according to the type of pruritus, from those with intractable eczematous changes (moderate or severe lichenification) of varying duration to those with pruritus caused by parasites, or secondary to antibiotic therapy, or associated with anxiety states.

Hydrocortisone was ineffective in patients with refractory pruritus without cutaneous changes, these patients

as a group being neurotic, and in those with pruritus due to parasites. Otherwise it is said to be a " valuable symptomatic agent ". It was applied in a 2·5% lotion or cream until some relief was noted, when a 1% preparation was used. The lotion was less effective than the cream.

John T. Ingram

DERMATITIS

1411. **Results of Oral B.C.G. Vaccination Administered in Repeated Doses at Intervals to Patients with Cutaneous Tuberculosis and Similar Diseases.** [In English]
L. Baptista and N. Belliboni. *Dermatologica* [*Dermatologica (Basel)*] **110**, 132–143, Feb., 1955. 10 figs., 39 refs.

At the Hospital de Clínicas, São Paulo, Brazil, patients with cutaneous tuberculosis, erythema induratum, and lupus erythematosus were given B.C.G. vaccine by mouth in a dosage of 0·1 to 0·3 g. weekly, sometimes divided and given every other day. In some patients the Mantoux reaction became less sensitive. Two patients with erythema induratum, one with scrofuloderma, and 4 with lupus erythematosus improved with treatment.

[From such a small series—7 cases—with no adequate follow-up no conclusions concerning the efficacy of this treatment can be drawn.] *S. T. Anning*

1412. **The Topical Application of *iso*Nicotinic Acid Hydrazide in Tuberculosis of the Skin**
G. Harvey and G. Leslie. *British Journal of Dermatology* [*Brit. J. Derm.*] **67**, 225–226, June, 1955. 6 refs.

Six cases of lupus vulgaris and 3 cases of verruca necrogenica responded to treatment with an ointment containing 5% *iso*nicotinic acid hydrazide. Four of the cases of lupus vulgaris were treated over a year ago and one 9 months ago, and so far no signs of fresh activity have been seen. In a condition such as this the follow-up has been relatively short and the favourable results are at present only provisional.

Although the number of cases is small, the results indicate that the topical use of *iso*nicotinic acid hydrazide may have a place in the treatment of these and allied skin diseases and more extensive trials appear to be fully justified. All the cases of Bazin's disease treated in the same way became worse and the topical use of the drug in this condition may prove to be contraindicated.—[Authors' summary.]

1413. **The Effects of Stilboestrol on the Surface Sebum and upon Acne Vulgaris**
A. Jarrett. *British Journal of Dermatology* [*Brit. J. Derm.*] **67**, 165–179, May, 1955. 7 figs., 39 refs.

At University College Hospital, London, stilboestrol in a dosage of 1 mg. three times a day was given to 6 patients suffering from acne; in one case the dose had to be reduced to 1 mg. daily because of nausea. In all cases the acne improved, and during treatment there was a significant reduction in the amount of sebum on the surface of the skin; the higher the initial level of sebum, the greater the daily reduction. Usually the amount of sebum on the surface of the skin tended to return to the pre-treatment level when hormone therapy was discontinued. Histochemical examination of biopsy material taken before and after administration of the stilboestrol did not reveal any changes in the nature of the fat or in the glycogen content of the sebaceous glands.

Of another series of 43 patients with acne who received stilboestrol by mouth 32 improved, though there was some tendency to relapse after cessation of treatment.

E. Lipman Cohen

DERMATOSES

1414. **Studies on Sweat Retention in Various Dermatoses**
F. E. Cormia and V. Kuykendall. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **71**, 425–435, April, 1955. 6 figs., 10 refs.

A recent experiment having shown that in patients with dermatitis the local sweating response to the intradermal injection of methacholine was diminished in the affected areas as compared with normal areas of skin, the authors have extended the investigation to 27 patients with various dermatoses at the New York Hospital. The amount of sweating was determined by a modified starch–iodine procedure on both normal and affected areas of skin before and after the intradermal injection of methacholine. In addition the skin temperature, *p*H, and electrical resistance were determined and biopsy specimens of skin were taken for study from over half the patients both before and after the intradermal injection.

In patients with eczematous eruptions a significant degree of sweat retention was frequently present, and aggravation of the eruption by exposure to heat was well correlated with the calculated degree of sweat retention. In the presence of sweat retention the sweat glands appeared to be normal and the dermal portion of the sweat ducts showed no significant abnormalities other than inconstant dilatation. In cases of psoriasis, hypertrophic lichen planus, and various types of eczematous dermatitis sweat retention appeared to be caused by obstruction of the upper epidermal portion of the sweat duct.

The authors also studied the depletion of glycogen from sweat glands and sweat ducts after injection of methacholine. The accumulation of Schiff-positive-staining material in the upper epidermal portion of the sweat duct during sweat retention is described.

[This very interesting paper must be read in the original for details of the methods used and the results achieved.]

S. T. Anning

1415. **The Psychogenic Origin of Psoriasis.** (Origine psychogène du psoriasis)
M. Bolgert and M. Soulé. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **82**, 252–266, May–June, 1955. 12 refs.

A careful study of 200 patients with psoriasis at the Hôpital Saint-Louis, Paris, showed that emotional factors were important in at least 90% of them. Over half of them had the mental make-up which Janet called " psychasthenia ", which is characterized by over-meticulousness and a need for repeated verification; the

authors make the interesting observation that over 15% of their patients were employed on some type of accountancy work, an occupation eminently suited to their temperament. These patients are also prone to superstition, but severe obsessional symptoms and melancholia are rare though anxiety is common; in contrast to the psychasthenics, 38 patients suffered from anxiety states. In more than two-thirds of the total, exacerbations were psychogenic in origin, the nature of the disturbance being usually manifested by a feeling of aggression or frustration.

The improvement in the psoriatic condition so often seen during the war was due to the well-known general improvement in psychasthenic states which is apt to occur when a real danger is met and when freedom of choice of action is limited. A hereditary factor appeared to be present in 37 patients. Itching occurred in 78 of 92 patients who were questioned specifically on this point, but it was rarely complained of spontaneously. In a few others there was a feeling of burning of the lesions, which was usually transient and was increased by contact with clothes. The improvement in psoriasis often noted after ultraviolet irradiation or in pregnancy may be due to their tonic effect on the emotions. In some cases the site affected is significant; thus psoriasis may affect the external genitalia when the cause has a sexual origin, while if the trouble is connected with the patient's work the limbs are apt to be affected. Finally, when the stimulus to the eruption lies in an unhappy outcome to an " affair of the heart " the scalp and retro-auricular areas suffer.

The authors conclude by suggesting that psoriasis is due to the formation of a specific substance (whose nature is unknown) in the nervous system, probably in the brain; this same substance causes also psoriatic erythrodermia and arthritis. The logical inference is drawn that main form of treatment in many cases should be psychotherapy. *E. Lipman Cohen*

1416. **Trial of Procaine and Atropine in the Treatment of Psoriasis.** (Therapeutische Versuche bei Psoriasis mit Novocain und Atropin)
L. HELMECZI. *Dermatologica* [*Dermatologica* (*Basel*)] **110**, 439–448, June, 1955. 20 refs.

1417. **Dapsone in Dermatitis Herpetiformis**
J. K. MORGAN, C. W. MARSDEN, J. G. COBURN, and J. M. MUNGAVIN. *Lancet* [*Lancet*] **1**, 1197–1200, June 11, 1955. 20 refs.

The authors treated 28 patients suffering from dermatitis herpetiformis at the Manchester and Salford Skin Hospital with dapsone (4:4′-diaminodiphenyl sulphone). Most of the patients had already undergone treatment with arsenic or with sulphapyridine for periods up to 7 years, with varying degrees of control. Dapsone was given for at least 3 months. According to the intensity of the eruption and to the response to treatment the daily dose of dapsone varied between 50 and 100 mg. In 23 cases (82%) the disease could be successfully controlled. In the remaining cases the response was less well marked—the itching persisted, although its intensity was reduced, and the skin never became completely free of lesions. Of the 23 patients who had previously been treated with sulphapyridine, the response to dapsone was better in 10 and the same in 12. Many patients preferred treatment with dapsone because it relieved the itching more rapidly. Routine haemoglobin estimations were carried out periodically in all cases, and liver function tests after 3 months' treatment. A slight decrease in the haemoglobin content of the blood was observed in 6 cases, and 2 patients became cyanosed. Slight abnormalities in the results of the liver function tests were detected in 6 cases. The concentration of dapsone in the blood was determined in 6 cases and that in the skin in 4; no evidence of selective concentration of dapsone in the skin, as has been suggested by other workers, could be found.

The authors conclude that dapsone is now the drug of choice in the treatment of dermatitis herpetiformis, although sulphapyridine appears to be more effective in a few cases. *A. Fessler*

1418. **Dapsone in the Treatment of Dermatitis Herpetiformis**
J. O'D. ALEXANDER. *Lancet* [*Lancet*] **1**, 1201–1202, June 11, 1955. 10 refs.

The author, working at the Glasgow Royal Infirmary, investigated the efficacy of dapsone in the control of dermatitis herpetiformis in 28 cases. An initial dose of 200 mg. daily was given for the first week, followed by 100 mg. daily for 2 weeks. When necessary the initial dose was increased to 300 mg. daily, given for 2 weeks, but if there was still no response the treatment was stopped. The dosage was gradually reduced until the minimum maintenance level was established. A daily dose of 100 mg. was usually sufficient to keep the disease under control, but individual requirements varied considerably; 2 patients needed only a single dose of 100 mg. weekly. Four patients did not respond to the treatment; in the remaining 24 cases the disease was successfully controlled for periods ranging from 5 months to more than a year. In most cases a relapse occurred when dapsone was stopped.

Cyanosis developed in 18 cases (severe in 7), and in 3 cases the haemoglobin level fell by more than 10%. In one case the blood urea level rose above normal, and in 3 cases the result of the thymol turbidity test indicated a temporary liver dysfunction. Other toxic side-effects [regarded by the author as trivial] were nausea, headache, dyspnoea, palpitation, and tiredness; each of these effects was observed in a few cases only. Patients with experience of both sulphapyridine and dapsone generally preferred the latter. The author regards dapsone and sulphapyridine as equally effective in the control of dermatitis herpetiformis, but prefers the former because it seems to produce less severe toxic effects. The treatment, however, must be carefully controlled by means of frequent haemoglobin estimations.

[The high initial dose may perhaps explain the higher incidence of toxic side-effects in this series than in the series reported by Morgan *et al.* (see Abstract 1417). *A. Fessler*

Paediatrics

1419. **Hypertrophic Pyloric Stenosis in the Premature Infant.** (La sténose hypertrophique du pylore chez le nourrisson prématuré)
G. Van Ooteghem. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **44**, 263–271, May, 1955. 2 figs., 15 refs.

Congenital pyloric stenosis is generally considered to be rare in premature infants: the author, however, encountered 17 such infants among a total of 703 cases (2·42%) of pyloric stenosis treated between 1922 and 1942 at 3 hospitals in Stockholm and one in Göteborg. As with full-term infants the majority of the affected premature babies were boys (82%), and 65% were first-born. Typical projectile vomiting started most frequently in the fifth week, and in 6 cases the onset was considered to be before the date of full term.

The signs were the same as those observed in full-term infants, except that gastric peristalsis was less constant. The palpation of a tumour was regarded as of minor importance, the diagnosis being established radiologically. Only one infant was treated surgically (after unsuccessful medical treatment) and he died. One recovered spontaneously[!] The average time the infants were kept in hospital was 51·5 days.

[This paper perpetuates the differences between Swedish and British paediatricians with regard to the diagnosis and treatment of pyloric stenosis. Diagnosis by palpation of the tumour and treatment by operation, as generally practised in Great Britain, necessitate only a few days in hospital and do not requre *x*-ray examination. However, the article is valuable in drawing attention to the occurrence of pyloric stenosis (and of pyloric spasm) in premature infants.] *Wilfrid Gaisford*

1420. **Thrush Oesophagitis with Pharyngeal Incoordination Treated with Hydroxystilbamidine**
O. H. Wolff, B. W. Petty, R. Astley, and J. M. Smellie. *Lancet* [*Lancet*] **1**, 991–995, May 14, 1955. 2 figs., 34 refs.

Two cases of severe thrush oesophagitis in newborn infants are reported from the Children's Hospital, Birmingham. Both infants were thought to be moribund when treatment with hydroxystilbamidine was started, but both made a complete recovery. A trial of hydroxystilbamidine was suggested by the success achieved with this drug in other mycotic infections.

In both children there was incoordination of swallowing, demonstrated by fluoroscopy, which was largely restricted to the pharynx and did not involve the oesophagus itself. The authors suggest that such incoordination probably accounts for the pneumonia which is a frequent terminal event in cases of severe thrush infection; pneumonia developed in one of the cases described. Clinically the disorder of swallowing was manifested by dribbling of milk or by vomiting, which was sometimes projectile. During feeds there were attacks of cyanosis which were shown by fluoroscopy to be due to the entry of milk into the respiratory tract. It is pointed out that since incoordination of swallowing may persist for several days after the thrush membrane has disappeared from the mouth it is inadvisable to resume oral feeding until swallowing has been shown by fluoroscopy to be normal. Secondary pyogenic invasion is a frequent complication, and additional administration of an antibiotic is recommended.

Hydroxystilbamidine causes pain and necrosis when given intramuscularly, and in the 2 cases reported, therefore, it was given intravenously in a dosage of 5 mg. per kg. body weight every 12 hours for 6 and 4 days respectively. (A third successfully treated case is noted in an addendum.) *Marianna Clark*

1421. **Pseudomembranous Enterocolitis in Infancy**
E. C. Beatty and C. R. Hawes. *Journal of Pediatrics* [*J. Pediat.*] **46**, 654–662, June, 1955. 4 figs., 17 refs.

1422. **Heart Failure in Infancy with Abnormalities of the Valves and Endocardium**
J. J. Kempton and L. E. Glynn. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 191–202, April, 1955. 15 figs., 20 refs.

The authors describe in some detail the cases of 3 infants who died at the Canadian Red Cross Memorial Hospital, Taplow, Bucks, of cardiac failure between the ages of 5 and 8 months, since in all 3 the symptoms and signs were misinterpreted initially or recognized late.

In every case the infant was first seen for dyspnoea on feeding, accompanied by spasmodic choking. The blood pressure and respiratory rate were high, there was some oedema, and the liver was enlarged. At necropsy the heart was found to be greatly enlarged. Other post-mortem findings, which differed only slightly in the 3 cases and are described in detail for each, included thickening of the endocardium, and ventricular or atrial hypertrophy, one or more of the valves being affected in all cases. In the 3rd case the tricuspid valve showed a myxomatous-like thickening (which is well illustrated in one of the photomicrographs that are reproduced in the paper).

The authors discuss the difficulty of diagnosis of cardiac failure in infancy, emphasizing the ease with which it may be confused with pneumonia and laying weight on the finding of an enlarged liver. They stress the importance of giving digitalis in these cases. A review of other cases of cardiac fibro-elastosis reported in the literature suggests that valvular involvement occurs in one-third to one-half of all such cases, but the incidence may be even higher. The cause of the condition is not known, but the authors support the hypothesis put forward by Johnson (*Arch. Path.* (*Chicago*), 1952, **54**, 237; *Abstracts of World Medicine*, 1953, **13**, 336) that it is a reaction of a normal endocardium to anoxia due to a

congenital abnormality of the heart, to premature closure of the foramen ovale, or anaemia in the mother.

[This article is notable among other qualities for the excellence of its illustrations.] *H. G. Farquhar*

1423. **A Contribution to the Study of Interstitial Plasma-cell Pneumonia.** (Beitrag zur interstitiellen plasmazellulären Pneumonie)

E. Reisetbauer and O. Braun. *Österreichische Zeitschrift für Kinderheilkunde und Kinderfürsorge* [*Öst. Z. Kinderheilk.*] **11**, 286–301, 1955. 5 figs., 37 refs.

This is an epidemiological, pathological, and clinical study of an institutional epidemic of interstitial plasma-cell pneumonia which involved 32 babies. The youngest patient was 7 weeks old at the time of onset and the oldest 26 weeks, the highest incidence being at the age of 13 weeks. All except one were premature infants, and the only full-term baby was grossly dystrophic. The epidemic showed a definite progression to a peak, followed by a rapid fall in incidence. Simultaneous onset in several children was seen occasionally, and in contacts repeatedly. Closing and disinfection of the wards was followed by a complete disappearance of the disease from the hospital. Cultures of sputum, urine, and faeces yielded the same organisms as in controls, but *Pneumocystis carinii* was found in the lungs in 10 out of 13 fatal cases which came to necropsy and in none of the control cases examined at the same time. Therapeutic experiments were disappointing but the measures of prevention taken appeared to be entirely successful.

H. S. Baar

1424. **The Treatment of Interstitial Plasma-cell Pneumonia.** (Zur Therapie der interstitiellen plasmazellulären Frühgeburtenpneumonie)

K. Eberle, A. Rett, and N. Rümmele. *Österreichische Zeitschrift für Kinderheilkunde und Kinderfürsorge* [*Öst. Z. Kinderheilk.*] **11**, 194–201, 1955. 7 refs.

The authors accept the protozoal nature of *Pneumocystis carinii* and consider it to be the causative organism of interstitial plasma-cell pneumonia, infection probably being airborne. Satisfactory results were obtained in a series of 25 cases at a children's hospital in Vienna by treatment with chloramphenicol, 15 of the infants surviving, which compares favourably with the high mortality reported in other series. The diagnosis in all 10 fatal cases in this series was confirmed by post-mortem examination. *H. S. Baar*

1425. **Three Cases of Interstitial Plasma-cell Pneumonia in Older Children.** (Drei "Altersfälle" von interstitieller plasmazellulärer Pneumonie)

J. Herbich. *Österreichische Zeitschrift für Kinderheilkunde und Kinderfürsorge* [*Öst. Z. Kinderheilk.*] **11**, 202–209, 1955. 19 refs.

A report is presented from the Pathological Institute of the University of Vienna on 3 fatal cases of interstitial plasma-cell pneumonia which developed at a considerably later age than usual, the patients being 5½, 6, and 9 months old respectively at the time of death. Two of the infants were born at full term and the third was 6 weeks premature. All three were seriously ill from other causes before they developed the pneumonia, one suffering from cellulitis, enteritis, and otitis media, the second from cellulitis, craniotabes, and gastroenteritis, and the third from an unspecified reticulosis. *Pneumocystis carinii* was found in the lungs in all three cases. The author expresses no opinion as to whether this organism is a protozoon or a yeast, but states that he failed to obtain the red staining of chromatin granules with Giemsa's stain which is usual in protozoa. [However, in view of the different findings of other authors and the difficulties often experienced with Giemsa's stain in histological sections, no great significance can be attached to this statement.] For demonstration of the organism the author recommends particularly a modified Gram stain and Gridley's chromate–leucofuchsin stain.

H. S. Baar

1426. **Acute Cerebellar Ataxia in Children.** [In English] G. Berglund, H. O. Mossberg, and B. Rydenstam. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **44**, 254–262, May, 1955. 6 refs.

During the first 9 months of 1953 poliomyelitis and influenza infections of Types A and B were common in Sweden. During this period 6 children aged 15 months to 5 years, who had all been neurologically healthy before the sudden onset of their symptoms, were admitted to three different Stockholm hospitals with signs of acute cerebellar ataxia. By the time of their admission to hospital, that is, between the 2nd and 14th days of the illness, all were afebrile and none had meningism, but nystagmus was present in 3 cases. It was found that 3 of the children had pure cerebellar ataxia, the 4th had "marked agitation of the head and the extremities" which persisted in a milder form for a year, while the last 2 cases were more severe and showed additional features. One of these patients was somnolent, showed rigidity of the extremities and extensor plantar responses, and had two convulsions late in the course of the disease, followed by temporary aphasia. The cerebrospinal fluid and the electroencephalogram (EEG) became abnormal during the second and third weeks of the disease, but later both gradually returned to normal. Five months later the child, although better, had not completely recovered and still suffered from slight spasticity of his legs and jerky speech. The last patient, a boy aged 4 years, had muscular pains at the onset of the disease, and when these subsided paresis of the lumbar musculature and ataxia became apparent. He made a complete recovery, although the EEG showed transient dysrhythmia. This case was considered to be atypical of cerebellar ataxia.

The authors consider that 2 of these cases were proven cases of poliomyelitis because the virus of Type 1 (Brunhilde) was recovered from the faeces, neutralizing antibodies against poliomyelitis Type-1 virus were established, and complement fixation occurred in significant titre in tests on the same virus. The last case described was also considered to be one of poliomyelitis because of the temporary paresis, although culture for Type-C virus was negative and serological

tests were not performed. In the 3 remaining cases the complement-fixation reactions were positive against influenza A or B, but significant changes in titre were not demonstrated; no proof was therefore obtained that influenza was the aetiological factor in these cases. (In 2 of these cases no tests for poliomyelitis virus were performed.)

The clinical picture in the " proven " cases of poliomyelitis was milder than in those of suspected influenzal aetiology. It is pointed out that poliomyelitis occasionally exhibits cerebellar ataxic features and it is considered that other pathogenic micro-organisms, such as the influenza virus, may also be aetiological agents in the production of acute cerebellar ataxia. Occasionally, however, a neoplasm in the posterior fossa may produce very similar clinical features.

[It has been stated by Ford (*Diseases of the Nervous System in Childhood*, Oxford, 1952, p. 470) that " acute cerebellar ataxia without any typical manifestations of poliomyelitis is probably never a result of Heine–Medin disease ". The isolation of poliomyelitis virus and changes in antibody titres during an epidemic of poliomyelitis are fairly commonly demonstrable in the general population. For this reason the authors' contention that the poliomyelitis aetiology in their non-paralytic cases is proven cannot be fully accepted until further evidence has been accumulated.] *John Lorber*

1427. **Cases of Cerebral Palsy in a Series of Mentally Defective Twins**
G. ALLEN. *American Journal of Mental Deficiency* [*Amer. J. ment. Defic.*] **59**, 629–639, April, 1955. 4 figs., 7 refs.

Of 551 inmates of the New York State Schools for Mental Defectives who were derived from 493 sets of twins and triplets, 60 had cerebral palsy, the diagnosis in 27 cases being congenital cerebral spastic palsy and 33 being regarded as cases of mental deficiency due to injury at birth. [The method of distinguishing the one group of cases from the other is not stated.] The frequency of twins among all patients with congenital spastic palsy admitted to the schools during the period 1948–52 was found to be the same as that in the general population (2%), suggesting that the condition does not affect twins more often than single-born infants. Among patients with mental deficiency due to birth injury, however, there were 5·3% of twins. On the other hand the other twin had died at or soon after birth in a significantly larger proportion of the cases of congenital spastic palsy (41%) than of those of mental deficiency due to birth injury (26%), the figure for twins with mental defect due to other causes being only 12%. The intelligence in cases of congenital spastic palsy tended to be lower than that in cases of cerebral palsy due to birth injury both in twins and in single-born children.

A consecutive series of 95 twin defectives was examined personally by the author; 11, belonging to 10 pairs, had motor impairment of cerebral origin; 3 of the pairs were monozygotic, one being the pair of which both members were affected, both having spastic diplegia. Of the other monozygotic pairs, one member of one had mental impairment due to kernicterus, while the other pair had a deficiency of plasma thromboplastin component which resulted in intracranial haemorrhage after birth in the aftercoming twin. *J. Foley*

1428. **Infantile Spastic Hemiplegia. III. Intelligence**
M. A. PERLSTEIN and P. N. HOOD. *Pediatrics* [*Pediatrics*] **15**, 676–682, June, 1955. 27 refs.

1429. **Masklike Facies with Associated Congenital Anomalies (Möbius Syndrome). Report of Three Cases**
A. NISENSON, A. ISAACSON, and S. GRANT. *Journal of Pediatrics* [*J. Pediat.*] **46**, 255–261, March, 1955. 7 figs., 12 refs.

The essential characteristics of the Möbius syndrome are facial paralysis (which may be unilateral or bilateral, complete or partial), unilateral or bilateral abductor weakness of the eyes, congenital abnormalities of the extremities, and, in some cases, involvement of other parts of the musculature of the head, neck, and upper arm.

In this paper are described 3 cases of this syndrome seen at the Children's Hospital, Los Angeles. In the first case, that of a girl, the abductor and adductor muscles of both eyes and the muscles of both sides of the face were affected; there was bilateral club-foot with webbing of the toes; 2 toes of the left foot were absent. In the second patient, a boy, the abductor muscles of both eyes and the facial muscles on both sides were involved; there were also bilateral coxa valga and shortening of the right leg and foot. In the third patient, also a boy, again the abductor muscles of both eyes and the facial muscles on both sides were involved; there was left-sided club-foot. All 3 patients were of normal intelligence.

The authors state that there appears to be no familial or hereditary tendency in cases of true Möbius syndrome; none of the patients' relatives in this series was affected in the same way. They cite from the literature instances of facial diplegia alone occurring in 2 or more members of a family. *C. O. Carter*

1430. **Manic-depressive Disease in Children**
J. D. CAMPBELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 154–157, May 21, 1955. 13 refs.

It is the author's view that in many adult cases of manic-depressive psychosis the symptoms date back to childhood. The case histories of 3 children with manic-depressive symptoms are reported; in 2 of these cases the child's mother had similar symptoms. It is claimed that at least 75% of children who are fearful of going to school but are otherwise well-adjusted are really suffering from endogenous depression and should be treated accordingly. The author considers that it is a mistake to attribute all emotional disturbances in children to environment, and that more attention should be paid to constitutional and genetic factors and to the child's family and relatives, not so much from the point of view of environment as from that of inherited characteristics. *R. S. Illingworth*

Industrial Medicine

1431. Radiation Cataract in Industry. Review of the Literature, Discussion of the Pathogenesis, and Description of Environmental Conditions in an Iron Rolling Mill

G. F. KEATINGE, J. PEARSON, J. P. SIMONS, and E. E. WHITE. *Archives of Industrial Health* [*Arch. industr. Hlth*] **11**, 305–314, April, 1955. 5 figs., 25 refs.

A review of the literature of radiation cataract as an occupational hazard is followed by the report of an investigation into the incidence of lenticular changes among workers in a British iron-rolling mill, where the intensity of infrared radiation at various stages of the process ranged from 0·02 to 0·10 cal. per sq. cm. per sec. The authors examined the eyes of 44 of the employees who had worked for long periods exposed to the glare of red-hot metal and who had never used any eye protectors and compared the findings with those in 104 controls fairly well matched for age. The classic posterior cortical changes of radiation cataract were found in 3 of the employees—all over 65 years of age—while posterior capsular changes were noted in 26. None of the control group showed posterior cortical changes but in 16 there were posterior capsular changes. The findings appear to indicate that these changes are not necessarily pathognomonic of radiation effects. In one particular rolling mill there had been only 2 doubtful cases of radiation cataract over a period of 30 years, and the authors conclude that only a small proportion of workmen exposed to infra-red irradiation develop radiation cataract and that the incidence of the condition is decreasing in the United Kingdom. *R. E. Lane*

1432. Radiological Changes in Pneumoconiosis Due to Tin Oxide

A. J. ROBERTSON and P. H. WHITAKER. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **6**, 224–233, April, 1955. 17 figs., 8 refs.

Tin is a metal with a high atomic weight (119) and consequently a high degree of radio-opacity [approximating to that of iodine]. Consequently, inhaled dust containing tin may produce the radiological picture of pneumoconiosis without there necessarily being any fibrosis. Only 12 cases of tin pneumoconiosis have been reported previously. The authors, working at the Liverpool Royal Infirmary, have examined 215 employees of a tin smelting works clinically and radiologically. In 121 of these subjects abnormal *x*-ray changes were present in the chest, varying from faint early mottling to gross dense nodulation. There was no evidence, in this series, of hilar lymph-node enlargement or progressive massive fibrosis. The *x*-ray changes varied with the length and type of exposure to tin.

The chest radiographs of men working in the ore house, where they were exposed to dust containing mainly tin oxide, showed multiple, hard, discrete opacities approximately 1 mm. in diameter, very numerous in advanced cases, and sometimes very similar in appearance to residual droplets of iodized oil after bronchography. There were also linear opacities, presumably due to tin in the sub-pleural lymphatic vessels. These lines were most marked at the bases, where they tended to run horizontally, but they also occurred in other parts of the lung fields including the apices. Similar linear opacities were present in the interlobar fissures, and also in the mediastinal pleura, where they sometimes outlined the heart or aorta.

Workers at the smelting furnaces, who were exposed to fumes of tin oxide rather than dust, showed different changes, the radiograph of the lung fields having a nodular appearance, with nodules about 3 to 5 mm. in diameter. These nodules were fewer and less dense than the opacities in the ore-house workers. After 30 to 40 years' exposure, however, the nodules were smaller and denser, appearing to have contracted in size. They then resembled those seen in ore-house workers, but were less numerous.

Clinically, the condition in all cases appeared to be benign, there being no significant symptoms referable to a pneumoconiosis. The possibility of a long-term hazard is, however, under investigation. *G. Ansell*

See also Respiratory System, Abstract 1346.

1433. The Treatment of Industrial Lead Poisoning with Calcium EDTA. (Terapia del saturnismo professionale con calcio E.D.T.A.)

A. ZAMBRANO and L. ROSSI. *Riforma medica* [*Rif. med.*] **69**, 397–403, April 9, 1955. 7 figs., 9 refs.

After a discussion of the mode of action of chelating agents in the displacement of unwanted heavy metals from the body, the authors describe, from the Institute of Industrial Medicine, University of Naples, the use of calcium ethylenediaminetetraacetic acid (Ca EDTA) for the removal of lead from the system of 6 patients suffering from occupational lead poisoning. The substance was given intravenously in a daily dose of 2 g. for a period of one week and was well tolerated. It had a remarkable effect on the urinary excretion of lead, which was usually greatest on the second or third day, the quantities of lead in 24-hour collections of urine for the 6 patients being increased as follows: (1) from 10 μg. before treatment to a maximum of 870 μg.; (2) from 300 to 600 μg.; (3) from 30 to 120 μg.; (4) from 36 to 600 μg.; (5) from 500 to 1,000 μg.; and (6) from 280 to 850 μg. There was little alteration, however, in the plasma lead content, which varied between about 20 and 60 μg. per 100 ml. Coproporphyrin estimations showed a decrease in the degree of coproporphyrinuria. The authors were favourably impressed with this form of treatment and recommend its wider use. *R. Wien*

Forensic Medicine and Toxicology

1434. **A Modified Absorption Technique of Determining the ABO Group of Bloodstains.** [In English]
S. S. KIND. *Vox Sanguinis* [*Vox Sanguinis (Amst.)*] **5**, 15–19, April, 1955. 2 refs.

The basis of the grouping of blood-stains is the absorption technique, whereby the stain is treated with a known antiserum, the agglutinating activity of which is then compared, usually in serial doubling dilutions, with that of a control specimen against known erythrocytes, any reduction in activity in the absorbed serum indicating the presence in the stain of the specific antigen. The author, writing from the Forensic Science Laboratory, Harrogate, criticizes this technique on the grounds that removal of half the agglutinating power of the serum will result in a change of titre by only one place, whereas removal of the other half may involve a change of up to 10 places (depending of course on the original titre). One means of overcoming this is to dilute all the antisera before use to a point where they only just give satisfactory agglutination, and to interpret removal of this minimum reaction as diagnostic of the presence of the antigen, but this interpretation may be fallacious owing to factors such as the presence of a little soap in the fabric or the non-specific absorption found even in clean cloth which may affect the reaction.

The author describes a modified technique which, he claims, preserves the advantages of the dilution technique and overcomes its disadvantages. The stain to be tested is extracted with isotonic saline and a control piece of cloth similarly extracted. Serial dilutions of Group-O antiserum are prepared, and to each tube is added an equal volume of stain extract. Similar tubes are set up with saline and with the control extract. After absorption for one hour at room temperature one drop of a 2% suspension of erythrocytes is placed in each tube, and the differences, if any, in the degree of agglutination seen in the three series at each dilution are determined microscopically. The author claims that this method has the advantage of reinforcing the agglutinating power of the higher dilutions of antiserum with agglutinins extracted from the stain, and consequently makes the test more sensitive. *Gilbert Forbes*

1435. **A New Treatment of Barbiturate Intoxication**
A. SHULMAN, F. H. SHAW, N. M. CASS, and H. M. WHYTE. *British Medical Journal* [*Brit. med. J.*] **1**, 1238–1244, May 21, 1955. 23 refs.

$\beta\beta$-Methylethylglutarimide (NP 13) and 2:4-diamino-5-phenylthiazole hydrobromide or hydrochloride (DAPT) are new therapeutic agents which have proved of value in reversing the toxic effects of barbiturate drugs. NP 13 is the more active and appears to offer a direct antagonism to the barbiturate molecule, to which it is chemically similar, while DAPT is a good synergist to NP 13 and also possesses a useful independent stimulating action on respiration. The combination of the two substances is less likely to produce toxic effects, such as hypertension, excitability, and convulsions, than is NP 13 alone. In this paper from the University and Royal Hospital, Melbourne, the authors describe 41 cases of overdosage with barbiturates, 9 of which were serious, which they successfully treated with these agents, there being only one death in the series.

The aim of treatment in such cases is to restore the patient from deep coma to a "safe state" of light narcosis in which muscle tone and reflexes, including the pharyngeal reflex, are present. The authors' method is as follows. After an endotracheal tube has been passed to test the pharyngeal and laryngeal reflexes the stomach contents are carefully aspirated and a 5% glucose intravenous infusion set up under antibiotic cover. Meanwhile 2·5 g. of NP 13 is dissolved in 500 ml. of normal saline at 80° to 90° C., the substance being only slightly soluble at normal temperatures; this solution after autoclaving is stable and active for 3 months. Since DAPT decomposes on autoclaving and in solution, 300 mg. of dry sterile powder is dissolved in 20 ml. of normal saline just before use as required. Into the tubing of the intravenous drip 1 ml. of DAPT solution, followed immediately by 10 ml. of NP 13 solution, is injected not more often than every 3 to 5 minutes, more rapid administration being likely to lead to toxic effects such as vomiting or retching and sometimes flickering of the fingers; if these appear they can be abolished by small intravenous doses of 2·5% thiopentone sodium. The authors have found that the safe state in a deeply comatose patient is generally reached in 2 hours, after an average total dose of about 200 ml. of NP 13 solution and 20 ml. of DAPT. Consciousness is usually regained within 8 hours of reaching the safe state. However, cases in a deeper stage of coma may require further treatment, especially when long-acting barbiturates are involved, as happened in 10 of the authors' cases.

The authors regard these drugs as a very useful advance in the treatment of barbiturate poisoning. By their use prolonged nursing and also prolonged endotracheal intubation are avoided, and the complications associated with continued coma are virtually abolished. The one fatal case in this series is described in detail, the authors concluding that death was not related to the specific treatment. *M. E. MacGregor*

1436. **Some Medico-legal Aspects of Aggression**
R. S. BANAY. *Journal of Forensic Medicine* [*J. Forensic Med.*] **2**, 83–85, April–June, 1955.

1437. **Hemolytic Transfusion Reactions. Medico-legal Aspects**
J. J. GRIFFITTS. *Journal of Forensic Medicine* [*J. Forensic Med.*] **2**, 78–82, April–June, 1955.

Anaesthetics

1438. **Anaesthesia and the Common Cold**
G. ELLIS. *Anaesthesia* [*Anaesthesia*] **10**, 78–79, Jan., 1955. 3 refs.

The presence in a patient of an upper respiratory infection is usually considered a good reason for the postponement of surgery. However, a search of the literature shows that no facts have ever been recorded to support this opinion. The common cold is a virus infection which affects the upper air passages but does not penetrate to the trachea or beyond. Immunity is short-lived, lasting not more than a month. An attack is almost always followed by a secondary infection of the paranasal sinuses; this is the real source of danger which the anaesthetist must consider in advising for or against postponement of operation.

If the patient needs his operation at once, then he must be regarded as fit for anaesthesia with, of course, careful choice of method according to the presence and nature of other conditions. The real problem arises when early operation is not essential, but is desirable for a variety of reasons. For example, it may have taken much persuasion to get the patient to enter hospital and postponement may mean abandonment; or postponement may be surgically or economically undesirable. In such circumstances, therefore, the author considers that " it may be worth while to run the risk of prolonging the illness postoperatively rather than to insist on the certainty of doing so preoperatively ", and he also asserts that " only in those cases where we are absolutely certain that no one will suffer at all by the postponement should the operation be put off till the cold has gone ".

The virus itself does not extend beyond the upper air passages, and with antibiotics and physiotherapy the risk of a secondary extension can be made very small. On the other hand the patient will probably acquire a cough, so it would be reasonable to postpone abdominal operations with a midline incision and operations for hernia because of wound strain. Moreover, surgery of the nose, throat, eyes, and thorax is obviously contraindicated. But apart from these exceptions, postponement on account of a common cold is generally unnecessary.

W. Stanley Sykes

1439. **Barbiturate Narcosis in Porphyria**
J. W. DUNDEE and J. E. RIDING. *Anaesthesia* [*Anaesthesia*] **10**, 55–58, Jan., 1955. 28 refs.

Porphyria is a little-known absolute contraindication to the use of barbiturates, especially thiopentone. There are three varieties. (1) Congenital porphyria, with photosensitivity of the skin and pigmentation of the bones and teeth, which is familial. (2) The cutaneous variety, with photosensitivity and recurrent skin lesions, often of a blistering type, caused by heat or minor trauma. This type also is familial. (3) Acute intermittent porphyria, in which attacks may occur spontaneously or are sometimes induced by drugs such as sulphonamides, sulphonal, barbiturates, and possibly alcohol. These may start with abdominal pain and distension, nausea, and vomiting, followed by the passage of red urine, and may lead to performance of laparotomy. Weakness follows in a few days, followed by a lower motor neurone paralysis, which may progress, with fatal involvement of the respiratory muscles, or may recover in 6 to 32 weeks.

From the Liverpool Royal Infirmary the authors report 37 attacks of acute porphyria in 32 patients, two-thirds of whom were women in the third or fourth decade of life. Paralysis occurred in 30 cases and was fatal in 10. In 15 cases an operation had recently been performed, thiopentone being known to have been given in 13; in all of these paralysis developed and in 5 it was fatal.

It is emphasized that thiopentone is absolutely contraindicated as an anaesthetic agent in all cases in which there is any suspicion of porphyria. When an emergency laparotomy is required thiopentone should not be given unless porphyria has been definitely excluded. All patients with the disease should be given a letter to be handed to the anaesthetist if any operation is proposed.

W. Stanley Sykes

1440. **Guillotine Tonsillectomy and Curettage of Adenoids under Ethyl Chloride Anaesthesia**
J. C. CAMPBELL and D. H. SMITH. *British Medical Journal* [*Brit. med. J.*] **1**, 1451–1453, June 18, 1955. 32 refs.

In this paper from the City General Hospital, Carlisle, the authors describe [and defend] the guillotine method of removing tonsils with curettage of adenoids under ethyl chloride anesthesia, stating that if carried out by an experienced surgeon, with the assistance of a competent anaesthetist, it is a satisfactory procedure. They have used the guillotine operation extensively on children up to the age of about 14 years with the exception of those in whom there was obvious peritonsillar fibrosis, when dissection was carried out. The only preoperative medication was a subcutaneous injection of $\frac{1}{100}$ grain (0·65 mg.) of atropine sulphate 45 minutes before the operation. The gag was not inserted before induction was started; the child was " coaxed " to sleep with nitrous oxide and then 5 to 10 ml. of ethyl chloride was introduced into the breathing tube. The authors emphasize that the operation requires an anaesthesia of considerable depth, and that the services of a competent anaesthetist who is aware of the dangers of ethyl chloride are essential. Between 1943 and 1952 the authors performed this operation on 12,038 children without a death. These results are contrasted with those in a reported series of 14,960 cases operated on between 1907 and 1920, in which there were 6 deaths.

E. D. Dalziel Dickson

Radiology

RADIOTHERAPY

1441. **Correlation of Field Size and Cancerocidal Dose in *X*-ray Treatment of Skin Cancer**
K. D. A. ALLEN and J. H. FREED. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1271–1274, April 9, 1955. 2 figs., 6 refs.

The well-known graphs of Strandqvist relating tumour dose to duration of *x*-ray treatment give no information on a point of particular importance in the treatment of cancer of the skin—the relation of field size to maximum dosage for the best cosmetic results. To fill this gap the authors have made a close study of 564 cases of primary cancer of the skin (basal-cell and squamous-cell carcinoma, including the lip), which were followed up for at least a year after treatment. In most cases radiation at 90 to 125 kV was used, with added filter of 1 to 5 mm. Al; a few were treated at 135, 200, and 250 kV. Single massive doses were used for the smallest lesions, especially in patients coming from remote districts. There was no indication that fractionation improves the cosmetic appearances if the field size is less than 1 sq. cm.

The tumour dose was taken as approximating to the skin and air dose for fields less than 1·2 cm. in diameter and 2 to 3 mm. thick; for larger fields, the skin and tumour doses were arrived at by calculation. Mild radiodermatitis was diagnosed in the presence of telangiectasia in an otherwise good scar; delayed healing or late necrosis was classed as severe radiodermatitis. Graphs were prepared by Strandqvist's method for various sizes of field, the tumour dose administered being plotted on double logarithmic paper against the duration of treatment for cases with good therapeutic and cosmetic results, and the slope of each was found to correspond to that determined by Strandqvist, following the equation $D_{e\cdot r} = \frac{D}{t0{\cdot}22}$, where $D_{e\cdot r}$ is the equivalent roentgen dose, given in a single treatment, producing the same biological effect as a dose D fractionated over t days. The quantity $t0{\cdot}22$, the fractionation factor, may thus be used to determined the total dose to be fractionated over t days to give the equivalent of any single massive dose.

The authors found the range of safe dosage to be much wider than that given by Strandqvist, but this range was directly related to field size. For fields over 1 sq. cm. the minimum single curative dose is 2,250 r, the same as Strandqvist's figure; for fields of less than 1 sq. cm. it is 3,000 r. The latitude of safe dosage increases markedly with fractionation; for example, in fields of less than 2 sq. cm. the range for a single dose is about 1,750 r, but for 12 days' fractionation it is 2,800 r. On the other hand latitude decreases as field size increases; for fields of more than 9 sq. cm. it is only 500 r for a single dose, or 1,200 r given over 10 days.

For the average case the dose proving the highest cure rate with fewest complications would be an average between maximum skin tolerance and minimum curative dose for the size of field. But treatment must be individualized and allowances made for such factors as age. Moreover, if collateral circulation is poor (as on the back of the hand, leg, or back), even the minimum curative dose may be too high and surgery may then be preferable. The curves apply principally to the face, neck, and lip. On the ear and nose, with underlying cartilage or bone, dosage should be rather lower and fractionation more. For the best results at least 90 to 250 kV should be available. *J. Walter*

1442. **Radiation Hazards in the Use of Thorium X for Skin Therapy**
S. J. WYARD, A. NIGHTINGALE, and I. G. AUSTIN. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 274–278, May, 1955. 2 figs., 4 refs.

1443. **Cancer of the Larynx. Five-year Results, with Emphasis on Radiotherapy**
C. C. WANG and A. R. O'DONNELL. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 743–747, May 5, 1955. 6 figs., 2 refs.

The therapeutic results obtained in 253 histologically proved cases of endolaryngeal cancer seen at the Massachusetts General Hospital between 1931 and 1949 inclusive are analysed, the period of follow-up being at least 5 years. The value of tomography in addition to laryngoscopy in the diagnosis of this condition is emphasized. Of the 253 patients, 240 (95%) were males, and in all except one squamous-celled carcinoma was found on histological examination. Treatment consisted in primary irradiation in 161 cases and surgical removal of the growth in 84; the remaining 8 patients were not treated.

The cases were classified according to the stage of the disease at the time of treatment, and the results are given in tables. It is clear that in early cancer of the larynx there is little to choose between surgery and irradiation, but the latter preserves the larynx and a useful voice; further, if irradiation is unsuccessful in early cases more radical treament can be carried out later. In cases of advanced cancer of the larynx without lymph-node involvement, especially in those with subglottic extension, surgery appears to be superior to irradiation. When the lymph nodes are involved the results with either method are very poor, but those obtained with irradiation are slightly better than those obtained with surgery.
R. D. S. Rhys-Lewis

1444. **The Performance of the Medical Research Council 8 MeV Linear Accelerator**
G. R. NEWBERY and D. K. BEWLEY. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 241–251, May, 1955. 19 figs., 11 refs.

1445. **High-pressure Oxygen and Radiotherapy**
I. CHURCHILL-DAVIDSON, C. SANGER, and R. H. THOMLINSON. *Lancet* [*Lancet*] **1**, 1091–1095, May 28, 1955. 4 figs., 12 refs.

In consequence of the work of Gray *et al.* (*Brit. J. Radiol.*, 1953, **26**, 638; *Abstracts of World Medicine*, 1954, **15**, 444), who showed that the sensitivity of tumour cells to irradiation was increased in mice breathing oxygen, the authors have carried out a preliminary investigation at St. Thomas's Hospital, London, in which 4 patients with carcinoma of the breast and 4 with carcinoma of the lung were given radiotherapy while breathing oxygen at a pressure of three atmospheres absolute (30 lb. per sq. in.; 2·11 kg. per sq. cm.). All the tumours were large and so made it possible for one-half to be irradiated under the experimental conditions and the other half under normal conditions. A single tumour dose of 1,000 to 1,500 r was given to each half and biopsy specimens were taken from 1 to 3 weeks later; experience gained in this study suggests that 7 to 10 days is the optimum time. In 7 cases there was histological evidence of greater damage to tumour tissue in the half irradiated in oxygen, while in the 8th case this could not be determined since no tumour cells in either field survived.

For the treatment, which was tedious and took up to 6 hours, the patient was placed inside a modified naval diving recompression chamber, which is described in detail. Irradiation was given through a "perspex" panel 1 inch thick at 250 kV, H.V.L. 1·7 mm. Cu, and 60 cm. F.S.D , the patient being anaesthetized to prevent the convulsions likely to occur under high oxygen tension. Bilateral myringotomy was previously performed to prevent rupture of the tympanic membranes and middle-ear haemorrhage, fine polythene tubes being inserted to keep the perforations patent during treatment. Contact was maintained with the patient by means of an electrocardiograph, an electromyograph from the upper lip to detect the possible onset of convulsions—which in fact did not occur—and a thermistor to record the respiratory rate, the leads from all these being connected to a cathode-ray tube; special precautions were taken to avoid the risk of sparking causing fire or explosion. After premedication anaesthesia was induced with pentobarbitone sodium in 5% solution given intravenously at 1 ml. per minute until consciousness was lost, 0·25 g. being usually sufficient, though one patient required 0·75 g. Pethidine (100 mg.) was then given through the same needle, followed by succinylcholine (50 mg.); in 2 cases, however, 50 mg. of chlorpromazine only was given with the pethidine.

After inflation of the lungs with oxygen the trachea was sprayed with 4% lignocaine and a large endotracheal tube passed, a metal airway being then inserted to prevent biting of the tube. Controlled respiration was applied, with 75% nitrous oxide and 25% oxygen, while the myringotomy was performed, after which the anaesthetic machine was disconnected and the patient allowed to breathe air. Finally a CO_2 absorber and the electrodes were connected and the patient placed in the compression chamber on a special metal trolley (illustrated). Compression was carried out slowly, taking about 10 minutes, radiation treatment averaged 40 minutes, and decompression 7 minutes for those with breast tumour and 15 minutes for those with cancer of the lung.

Brief histories of each case are given and theoretical considerations and technical problems are discussed. It has been shown that the radiosensitivity of cells increases up to three times, but not more, with increase in oxygen tension; it is thus suggested that different pressures may be required for the treatment of tumours with different circulatory conditions. The authors conclude that the results of this preliminary investigation have been such as to warrant a more extensive trial of this method.

G. E. Flatman

1446. **Experimental and Clinical Studies with Radioactive Colloidal Gold in the Therapy of Serous Effusions Arising from Cancer**
C. MOSES, E. KENT, and J. B. BOATMAN. *Cancer* [*Cancer (N.Y.)*] **8**, 417–423, March-April, 1955.

The authors have carried out a series of experimental and clinical studies at the University of Pittsburgh School of Medicine on the use of radioactive colloidal gold (^{198}Au) in the treatment of malignant serous effusion.

To determine the distribution and toxic effects of ^{198}Au five groups, each of 20 rats, were given intraperitoneal injections of ^{198}Au and five similar groups were given ^{198}Au intrapleurally. The dose used was 5 μc. per g. body weight. One group of each series was killed and examined 6 hours, and others 1, 4, 8, and 12 days respectively after the injection. Known weights of the tissues of various organs were ashed at 300° C. for one hour, and assayed with a Geiger counter under identical conditions. The greatest activity was detected in the thymus gland, liver, spleen, adrenal glands, and lungs. Pleural or peritoneal effusions were usually present, and in the former case the lungs were often compressed by the external pressure. Microscopical examination of the lungs showed a black pigment, consisting largely of gold particles, in the macrophages on the alveolar walls. Some reticulo-endothelial hyperplasia, with an identical pigment in the macrophages, was found in the spleen. The liver contained only a trace of the pigment in the Kupffer cells. Many of the thymus glands examined were atrophic, pigmented, and in a few cases, necrotic. No other organ was regularly affected. In further experiments 8 dogs were given intrapleural injections of ^{198}Au in a single dose of 5 mc. per kg. in 20 ml. of solution. All survived, and no serious changes were noticed in the blood; only local effects were found at necropsy 4 to 12 weeks later. Injection of 10 to 40 mc. of ^{198}Au immediately beneath the line of an incision into the peritoneal cavity in a further 6 dogs failed to affect the rate of healing after the incisions had been sutured. Five groups of mice with pulmonary tumours were given intrapleural injections of ^{198}Au. No obvious changes were produced in the tumours, and little change attributable to radiation was seen at a distance greater than 1 mm. beneath the pleural surface.

Colloidal ^{198}Au has been injected into the pleural or peritoneal cavity of 112 patients with recurrent pleural effusion and 51 with ascites due to carcinomatosis. In 6

cases the urine was examined, and only about 5% of the dose was found to be excreted in the first 72 hours. The usual dose given was 100 mc., but multiple doses were used if the fluid reaccumulated rapidly. About one-half of all the patients responded satisfactorily. Complications, which were rare, included a few cases of radiation sickness, diarrhoea following intraperitoneal administration, haematopoietic depression after repeated doses, and pleural thickening. A subcutaneous leak in one case was followed by nothing more serious than local tenderness for 6 weeks. The use of ^{198}Au appeared to be contraindicated in the presence of intestinal obstruction, pleural thickening without effusion, and in terminal cases. *A. M. Jelliffe*

RADIODIAGNOSIS

1447. **Mass Roentgenographic Screening as a Lung-cancer-control Measure**
L. W. Guiss. *Cancer* [*Cancer* (*N.Y.*)] **8**, 219–236, March–April, 1955. 15 refs.

A voluntary mass radiographic survey of 1,867,201 persons, constituting 45% of the population of Los Angeles County, was carried out in 1950 on 70-mm. film, a normal-sized radiograph being taken of all suspects. Those examined were found to be a representative sample of the total population of the county, except for some excess of young adults.

The presence of a tumour was suspected in 3,500 cases, the patients being enrolled in a Chest Tumour Registry. Only 24·7% were under 45 years of age, and it was noted that the proportion of such suspects in each decade rose markedly with age.

Most of the suspects sought medical care, but in only 40% of cases was a final diagnosis reached within 3 months—which is probably the maximum permissible time interval if bronchial carcinoma is to be cured. In the final analysis 80% of the suspect group proved to have some definite disease, and 20% to have a neoplasm, which in half was malignant. Of these cases of organic disease, only 40% were unknown before the survey. However, analysis of the 213 proved cases of bronchial carcinoma showed that 80% were not recognized before the survey, and of those found to be free of lymph-node or pleural involvement at operation, 97% were discovered by the survey. The survey was thus obviously very effective in uncovering tumours in their clinically silent phase when a surgical cure is most likely to be obtained. The 3-year cure rates obtained were higher than usual, being 35·8% among cases treated by resection and 11·3% for all cases, treated and untreated.

The author holds that the mass radiographic survey with prompt surgery on detection is the only technique available at present which is likely to reduce the mortality from bronchogenic carcinoma. He points out, however, that as a means of control of cancer of the lung a voluntary survey of the type described is inefficient, and that restriction of the survey to those over 45, and possibly further restriction to males, would provide a greater yield of cases at a much lower cost per case. Where, however, the survey is designed primarily for detection of tuberculosis, the cancer control aspect may be regarded as incidental. *Kenneth A. Rowley*

1448. **Bronchography with Dionosil in Pulmonary Tuberculosis**
C. Don. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.* (*Lond.*)] **6**, 189–200, Jan., 1955. 9 figs., 24 refs

Bronchography has been carried out in 90 cases of pulmonary tuberculosis at University College Hospital, London, the medium used being "dionosil", a watery suspension of an iodine compound closely related to diodone, which is rapidly absorbed and does not obscure the lung fields. The technique is briefly described. Of the 90 patients, 82 had a positive sputum and/or cavitation before chemotherapy was started, but in all the cases bronchography was deferred until the condition was stabilized, although the sputum remained positive in 14 and cavitation was still present in 30. In one case bronchography was followed by a transient increase in the disease process, which, however, responded to further chemotherapy. The author states that after this incident streptomycin was given throughout the period of bronchography as a precaution.

The medium generally failed to outline cavities but was valuable in revealing bronchiectasis, which was present in all except 19 of the cases. The significance of bronchiectasis in relation to the method of treatment of tuberculosis is discussed. There was nothing in the bronchograms to indicate whether the bronchiectasis was of a tuberculous or "non-specific" type, but they showed the extent and distribution of the affected segments and helped to determine the choice between thoracoplasty and resection in those cases in which surgery was contemplated.

The author regards the technique as safe and likely to yield valuable information concerning the influence of bronchiectasis on the prognosis in active tuberculosis.
A. M. Rackow

1449. **Pulmonary Appearances in Polyarteritis Nodosa**
B. Strickland. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.* (*Lond.*)] **6**, 201–208, Jan., 1955. 14 figs., 14 refs.

In this paper from St. Mary's Hospital, London, the author first points out that from experiments in animals and clinical observations it would appear that polyarteritis nodosa is a manifestation of anaphylactic hypersensitivity to various antigens. Pathologically, necrotizing, inflammatory, obliterative lesions of the small arteries are widespread throughout the body. Males are more commonly affected than females and the age incidence is usually 30 to 40 years. Fever is generally present either at the onset or later in the disease. The prognosis is poor, but some patients have benefited from administration of ACTH or cortisone, although the long-term results of this form of treatment have yet to be assessed.

Radiologically, the changes seen in the lung fields —apart from terminal manifestations of heart failure such as gross cardiac enlargement and pulmonary oedema —take the form of infiltrations of very varying pattern and sometimes of pleurisy with effusion. Six cases are

briefly reported and radiographs are reproduced. The lesions tend to be transient and migratory and there may be complete clearing of the lung fields between attacks. Post mortem there are multiple granulomata and areas of necrosis in the small vessels at different stages of development. The author discusses the radiological changes in relation to eosinophilia, which was a feature in 3 of the cases described; he considers that some of these may be of the same nature as "eosinophilic lung" but that multiple granulomata and, to a lesser extent, infarcts and small atelectases also play a part in creating the bizarre picture. *A. M. Rackow*

1450. The Left Lateral Oesophagram in Mitral Valvular Disease

J. M. McKAY and J. D. AITCHISON. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **6**, 209–213, Jan., 1955. 3 figs., 6 refs.

The investigation described in this paper from Aberdeen Royal Infirmary was undertaken to determine the relative values of the left lateral and the right oblique views in demonstrating left atrial enlargement in mitral valvular disease. In 55 cases of rheumatic mitral disease in which there was evidence of left auricular enlargement radiographs were taken in the routine right anterior oblique position and, at a distance of 6 feet (1·8 m.), in the left lateral position, the oesophagus being outlined with barium sulphate.

Critical review of the films showed that in 25 of the cases no difference between the two methods was detectable in the degree of oesophageal displacement. In 27 cases left auricular enlargement was more evident in the left lateral than in the oblique view, while in 3 the converse was noted. In one case the enlargement was shown in the left lateral view only. In all cases the lateral view showed enlargement. The authors thus confirm the findings of Jacobsen *et al.* (*Amer. Heart J.*, 1952, **43**, 423; *Abstracts of World Medicine*, 1952, **12**, 196) that the left lateral view is superior to the right oblique for routine use.

Discussing the value of the method in demonstrating left ventricular enlargement, the authors describe the presence of a translucent zone between the barium and the lower heart shadow in many cases of pure auricular enlargement. When an associated lesion is present which could be expected to cause enlargement of the left ventricle this translucent zone is less frequently seen. [The figures relating to this part of the investigation are suggestive but not convincing.] *A. M. Rackow*

1451. Lymphangiography by Radiological Methods

J. B. KINMONTH, R. A. KEMP HARPER, and G. W. TAYLOR. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **6**, 217–223, April, 1955. 10 figs., 4 refs.

The authors describe the method of *x*-ray lymphangiography developed at St. Bartholomew's Hospital, London. The lymph trunks are first made visible by the subcutaneous injection of 2 ml. of an 11% aqueous solution of patent blue into the interdigital webs of the foot or hand (0·5 ml. into each web) followed by massage of the part. A suitable lymph trunk is then dissected out, a bloodless field being obtained by posture or bandaging, and approximately 5 or 6 ml. of 70% diodone injected through a No. 18 hypodermic needle, care being taken to avoid extravasation. The radiographs should be taken within 5 minutes of the injection, non-screen film being used for the extremities and screen film for the thicker parts.

Normal lymph trunks maintain a uniform thickness, but bifurcate as they pass proximally, so that their number increases. In idiopathic lymphoedema there is no blockage, the lymph trunks being either beaded and varicose or narrower and fewer in number than normal, the usual branching being absent. In acquired lymphatic obstruction the lymph trunks can be traced to the site of obstruction and collateral vessels may be distinguished, but there is no dilatation. It is therefore considered that the dilated lymph trunks of congenital and idiopathic lymphoedema are of developmental origin. In order to explain the delay in appearance of oedema which commonly occurs in such cases it is suggested that the abnormal vessels may be just able to deal with the tissue fluids under ordinary conditions, but that some aggravating factor such as an insect bite, infected cut, or ligamentous strain produces an excess of tissue fluid which cannot be drained by the defective vessels, with the resultant formation of permanent oedema. *G. Ansell*

1452. A Criticism of Renal Angiography

T. E. NESBITT. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 574–583, April, 1955. 8 figs., 14 refs.

The author has attempted critically to assess the value of renal angiography on the basis of 200 cases at the University of Michigan Hospital, Ann Arbor, in which this procedure was carried out because the information obtained by accepted methods of investigation was an inadequate guide to further treatment. He points out that if renal angiography is "primarily concerned with exploration . . . before surgical intervention then it fulfills a need"; if it is to be helpful in other cases it must provide information which cannot be obtained by excretory and retrograde pyelography and which is significant for the clinical management of the individual case. A renal tumour can be differentiated with accuracy from a renal cyst by angiography, but since operation is always performed when either lesion is present the angiogram is redundant. The procedure has been found unsatisfactory in differentiating adrenal lesions and of little value in renal hypertension; in the latter condition the arterial spasm which often follows injection of contrast medium into the renal artery may be quite misleading in interpreting the angiogram. Biochemical tests are of more value than angiography in assessing renal function. Renal angiography is, however, helpful in polycystic disease and in cases in which there are intrinsic structural anomalies of the renal vessels. The author concludes that only in isolated, carefully selected instances is renal angiography justified, since it so often fails to reveal information which is helpful in treatment. *John H. L. Conway-Hughes*

See also Industrial Medicine, Abstract 1432.

History of Medicine

1453. **Leonhard Rauwolf.** (Leonhard Rauwolf)
F. W. RIEPPEL. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 653–655, April 22, 1955. 3 figs., 27 refs.

In this short biographical sketch of the life and times of Leonhard Rauwolf the author recalls that the name of this 16th-century physician and botanist has only again come into prominence since 1952, when the use of extracts of the plant named after him (*Rauwolfia serpentina*) was revived for the treatment of hypertension. He had, however, other claims to fame, being the first to describe the therapeutic effects, as distinct from the culinary uses, of coffee, and because his collection of porcelain forms a proof of the widespread use of porcelain coffee cups in the Near East, in which he travelled widely, publishing in 1582 or 1583 a book describing his experiences on a journey through Syria, Arabia, and Mesopotamia. This book can still be seen in the library of the Herbarium at Leiden. (Reproductions of two illuminated pages of the book accompany the paper.)

Rauwolf was born in Augsburg, but the actual dates of his birth and death are not exactly known. The author believes he was born in 1540 and died of dysentery in 1596, and not 1606 as is often stated. From his brother-in-law we learn that he married in 1565 one Regina Jung, a daughter of a medical family well known in Augsburg at the time, but thought to be originally from Zürich. He qualified M.D. at Bologna in 1556. He was elected to the College of Medicine of Augsburg in 1587 and became its dean in 1590. The city archives for 1587–8 show that for his services as " medical officer of health " (*Stadtarzt*) he was paid 187 florins, 30 crowns. As a Protestant he was compelled to relinquish this post in 1588, and went for a time to Linz in Austria and thereafter appears to have become a doctor to the Austrian army in Hungary.

The author then speculates as to whether Rauwolf ever really saw the plant to which his name was given. The French botanist Charles Plumier (1646–1704) is said to have first named the plant after Rauwolf in his book *Nova plantarum americanarum genera* published in 1703. The origin of the descriptive term " serpentina " is also discussed. The earliest traceable uses of this term were those by Peter Schoeffer of Mainz in 1484 and by Paracelsus in 1525. The earliest description of the plant now called *Rauwolfia* is said by the author to have been by the Portuguese botanist and physician Cristobal Acosta in 1578 who named it *Lignum colubrinum*. Nearly 200 years later reserpine, the active principle, is mentioned in his *Herbarii amboiensis auctuarium* by the Dutch botanist Georg Eberhard Rumpf (1625–1702), which was published in Amsterdam in 1755. From other accounts, however, it appears that Rauwolf did actually see the plant at Aleppo and added it to his herbarium.

The author concludes his paper with a plea for further information concerning such points as the year of Rauwolf's birth and the existence of any portrait of him.

I. M. Librach

1454. **Abduction of a Patient for Anatomical Purposes in 1681. From the Records of the Hôtel-Dieu, Paris.** (Krankenraub zu anatomischen Zwecken 1681. Aus den Akten des Hôtel-Dieu in Paris)
E. F. PODACH. *Medizinische* [*Medizinische*] No. 15, 547–550, April 9, 1955.

The history of medical anatomy is shadowed by the scandal of body-snatching. From the Middle Ages onwards and throughout Europe most famous anatomists were guilty of this practice or of condoning it. Fallopius, for example, was accused of misusing the favour of his ruler the Grand Duke of Tuscany by securing for himself not only the bodies of men condemned to death, but also the right to execute prisoners for the convenience of his research. The plundering of scaffolds and cemeteries was the mildest accusation levied against anatomists. It is recounted that the great Vesalius himself made frequent nocturnal excursions to the sites of gibbets, and others fought with rivals and relatives of the condemned in order to be the first to cut down the victims, sometimes even before they were dead. This befell Jack Sheppard at Tyburn in London, in 1724, who was cut down while still half alive and subsequently killed in a struggle for his body. These barbarities continued until the 19th century, particularly in Great Britain, where a practical knowledge of anatomy was demanded for examinations. Professional body-snatchers were the most reliable source of anatomical materal; amateur practitioners were apt to present surgeons with " corpses " which had the disconcerting ability to rise from the dead a few hours later, being in fact men picked up in the street in a drunken stupor. Only mild punishments were levied if the dead person's possessions and grave clothes were left in the coffin, so students were eager assistants in these forays. An end was put to the scandal by the trial of the notorious Burke and Hare in Edinburgh and the passing of the Anatomy Act of 1832, an earlier Bill having been opposed by the Royal College of Surgeons and described by the then Archbishop of Canterbury as superfluous. Sir Astley Cooper's comment was that there was no corpse, of however famous a person, which he could not obtain, and that the only effect of the Bill would be to increase the price of bodies.

One practice that British anatomists never seemed to have resorted to was to steal moribund hospital patients or sell the bodies from the mortuary. This, however, happened at the Hôtel-Dieu in Paris in 1681. The records show that two surgeons were believed to be implicated in stealing a dying patient one evening and abandoning him, still alive, on the banks of the Seine.

An investigation was held, but there is no record of subsequent punishment—probably because a public scandal was feared. About this time the clergy drew attention to the fact that bodies which were legally being taken for dissection at the Hôtel-Dieu were not able to receive Catholic burial. They therefore ordered that only corpses of heretics should be so used. There was also a general attempt to get Protestants into the hospitals in order to convert them to Roman Catholicism before they died, those resisting conversion running the risk of not receiving Christian burial. This practice, however, was abolished by an edict of Louis XV.

Ruth Hodgkinson

1455. **Amebiasis: its Early History**
G. G. STILWELL. *Gastroenterology* [*Gastroenterology*] **28**, 606–622, April, 1955. 7 figs., 23 refs.

In 1849 the Russian naturalist G. Gros described and illustrated parasites found in the tartar of teeth. These parasites are now considered to have been examples of *Entamoeba gingivalis*, and Gros is thus believed to have been the first to observe parasitic amoebae in man. Credit for being the first to see amoebae in the faeces is usually given to Wilhelm (or Vilém) Lambl, a Czech, on the strength of articles published by him in 1859 and 1860. Leuckart, as early as 1863, realized that the organisms pictured by Lambl could not be amoebae (they were in fact degenerating forms of trichomonads) and a critical appraisal of Lambl's original writings by Dobell in 1940 (*Parasitology*, **32**, 122) definitely disposed of Lambl's claim to priority. According to Dobell, the first description of amoebae found in human faeces was given by Timothy Richards Lewis of the Indian Medical Service in 1870. The true pioneer work in amoebiasis dates, however, from 1875, when Lösch, a German working in St. Petersburg, published an account of the morphology and typical movements of the parasites. Lösch also attempted to produce experimental amoebiasis in dogs, but was unable to establish the clinical pathogenicity of the organisms he had discovered. In 1885 Kartulis, working in Alexandria but writing in German, described certain strange objects which he referred to as "giant amoebae", which they certainly were not; in 1886 he published a more important study of 150 cases of dysentery and reported the finding of parasites in sections of intestinal ulcers. He considered the parasites to be the same as those described by Lösch and to be the cause of dysentery in his patients.

In 1887 one Jaroslav Hlava published an article in a rare Czech journal in which he described and pictured amoebae isolated from some patients with dysentery and reported the successful infection of the cat with amoebiasis by the intrarectal inoculation of stools from these patients. The title of his paper "O úplavici. Předběžné sdělení", which means "On Dysentery. Preliminary Communication", gave rise to one of the most fantastic episodes in medical bibliography. In a German abstract of Hlava's paper by the aforementioned Kartulis, the title of the article was given as the name of the author, and thus the name of the learned doctor "O. Uplavici" became established in the literature and was quoted and requoted until finally the error was exposed by the scholarly researches of Dobell. The first case of amoebiasis in the United States was reported by Osler in 1890. Drawings made by Osler of the organisms which he found are preserved in the Osler Library at McGill University (and are reproduced in this article). The classic account of amoebic dysentery by Councilman and Lafleur of Johns Hopkins appeared in 1891. Quincke and Roos in 1893 demonstrated for the first time that more than one species of amoeba could be present in the human intestinal tract; they also differentiated pathogenic from harmless forms, and were the first to describe amoebic cysts. Schaudinn's erroneous description (1903) of a supposed life cycle of amoeba led to considerable confusion, which was finally cleared up in 1911 by the work of E. L. Walker in the Philippines. In 1913 Walker and Sellards proved by means of experiments on human volunteers that amoebiasis in man was caused by the ingestion of cysts of *E. histolytica* and that *Entamoeba coli* was non-pathogenic. This brief history is presented as a typical example of the way in which scientific knowledge is slowly and painfully accumulated, and also as a warning of the dangers involved in failure to verify all bibliographical references by reference to the original.

W. J. Bishop

1456. **An Ophthalmic Case-book of Eighty Years Ago**
G. J. O. BRIDGEMAN. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 381–384, May, 1955. 2 figs.

1457. **The First Cases of Leukaemia Reported in the Medical Literature.** (A propos des premiers cas de leucémie, publiés dans la littérature médicale)
E. STRANSKY. *Scalpel* [*Scalpel* (*Brux.*)] **108**, 578–582, May 28, 1955. 18 refs.

1458. **Eighteenth-century V.D. Publicity**
H. MACGREGOR. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 117–118, June, 1955.

1459. **The History of Plague in New Zealand**
F. S. MACLEAN. *New Zealand Medical Journal* [*N.Z. med. J.*] **54**, 131–143, April, 1955. 8 refs.

1460. **The Story of Caroline Crachami—the "Sicilian Dwarf"**
J. DOBSON. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **16**, 268–272, April, 1955. 2 figs.

1461. **The Rheumatic Diseases in the Works of Rufus of Ephesus.** (Las afecciones reumáticas en la obra de Rufo de Efeso)
A. RUIZ MORENO. *Archivos argentinos de reumatología* [*Arch. argent. Reum.*] **18**, 11–44, Jan.–April, 1955.

1462. **Sir J. Y. Simpson and the Battle for Anaesthesia**
J. C. MOIR. *Oxford Medical School Gazette* [*Oxford med. Sch. Gaz.*] **7**, 49–58, 1955. 3 figs.

1463. **Barthélémy Cabrol.** (Barthélémy Cabrol)
L. DULIEU. *Scalpel* [*Scalpel* (*Brux.*)] **108**, 453–458, April 23, 1955. Bibliography.